

BILHARZIASIS IN THE SUDAN.

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INTRODUCTION.

Bilharziasis, or Schistomiasis, to use the proper generic term, has been defined as "a group of diseases caused by certain digenetic trematodes of the order Schistomatides, which inhabit the venous system of man in various tropical and sub-tropical countries."¹

It has, at times, been known under various synonymous names, as for example, Bilharzia Disease, Endemic Haematuria, Katayama Disease, Schistosoma Cattlei and others. These, for the most part, have been applied either at the whim of the particular investigator or because of the country of origin.

For the purpose of this thesis the terms Bilharziasis or Schistosomiasis will be used indiscriminately and may be taken to refer to the same disease.✓

GENERAL GEOGRAPHICAL DISTRIBUTION.

It is one of the most widely spread diseases known, extending between lat. 40 N. and lat. 40 S. and being endemic in large areas of Asia, Africa and South America.² In Asia it is prevalent in Central and South China, Korea, Japan, Arabia, Mesopotamia, Mauritius and Madagascar; in North Africa it is common in Morrocco, Algiers, Tunis and Egypt; in Central Africa it is endemic in the Sudan, Uganda, Rhodesia and West Africa; in South Africa it has been reported from the Cape, Natal and the Transvaal. Brazil, Venezuela and Dutch Guiana, in South America are widely affected.

Indigenous infection has been reported from Western Australia also, so that extension in that continent is a possibility to be reckoned with.³

Portugal is the only country in Europe, at present, definitely known to be infected.⁴

While Schistosomiasis is not so widely spread as Ankylostomiasis, of the two it is the more serious having regard to its clinical manifestations and its fatality. Egypt and China are the countries which suffer most heavily from this disease. It is estimated that there are 10,000,000 sufferers in China⁵ and 6,000,000 in Egypt.⁶

RECENT WORK.

From the date on which Bilharz discovered *Distoma Haematobium* in 1852, in the Portal vein of a patient, many industrious workers attempted to work out the aetiology of the disease, but no real progress was made until Katsurade first described *Schistosoma Japonicum* in 1904. Thanks to them and the more recent work of Fujinami and Namakura, Myairi and Suzuki, Leiper, Christopherson and more lately Faust, the aetiology of Schistomiasis has been placed on a sound basis with resultant benefits in the direction of prophylaxis and treatment. Their work, together with that of other investigators, will be referred to in more detail later in the text.

GENUS SCHISTOSOMA.

In the genus *Schistosoma* seven species are known. Two of these *S. Haematobium* and *S. Mansoni* occur in man alone as natural infections while two, *S. Japonicum* and *S. Bovis*⁷ occur in domestic animals, as well as man in the same endemic area. There is, however, still a doubt of the occurrence of *S. Bovis* in man.⁸

The other three *S. Bomfordi*, *S. Indicum* and *S. Spindalis*⁹ occur in domestic animals e.g. horse, sheep, cattle and other animals, although it is not improbable that they may, like *S. Bovis*, invade man. This may explain some of the sporadic cases which occur in

India.⁸

It is customary to regard three of them only as natural parasites, causing definite infections of schistosomiasis, in man. These are *S. Haematobium*, *S. Mansoni* and *S. Japonicum*, and they are recognised as the causal organisms respectively of Urinary (or Vesicular) Schistosomiasis, Intestinal Schistosomiasis and Oriental Schistosomiasis (*Schistosomiasis Japonicum*). Infections from *S. Haematobium* and *S. Mansoni* may occur in the one person.

All three have their definite endemic areas which are limited by the range of distribution of their appropriate intermediary hosts. *S. Japonicum* occurs in China in the Yangtse basin, and in the provinces of Hunan, Honan, Hupeh, Anhui and Kiangsi. In Japan it is prevalent in the provinces of Yameshi, Hiroshima, at Saga in the North Island, and in the village of Katayama (from whence it obtained its original name). Endemic foci also exist in the Southern Phillipines and Korea.

The geographical distribution of *S. Mansoni*, as far as it is known, extends from the Nile Valley, through Central and West Africa, the West Indies and South America.

The *S. Haematobium* is found in many parts of Africa, more particularly along the Eastern side as

far south as Port Elizabeth. It occurs in the Sudan, Uganda and Rhodesia, and also in West Africa. In North Africa it is common in Morrocco, Algiers, Tunis and Egypt, and occurs also in Arabia, Palestine, Persia, Mesopotamia, Cyprus, Mauritius, Reunion and Madagascar. It has been reported from West Australia.

Khalil¹⁰ has said that, as regards Egypt, *S. Mansoni* is limited to Lower Egypt and North of Cairo, and *S. Haematobium* to Upper, Middle and Lower Egypt. Certainly as far as our experience in the Sudan goes *S. Haematobium* would seem to be the principal Bilharzia parasite so far discovered.¹¹ Sporadic cases of *S. Mansoni* have been reported¹² in Mongolia, but it would seem from recent information that many more cases have been found in the White Nile Province. Perhaps future investigators will prove it to be much more prevalent than is at present realised.

GEOGRAPHICAL DISTRIBUTION IN THE SUDAN OF BILHARZIA.

Owing to its vast size, the wild nature of the country, its climate, the lack of water and roads, which present insurmountable difficulties to travellers, the savage, ignorant and primitive character of the sparse population, the short time it has been occupied, the development and opening up of the Sudan is not yet completed. This, together with scarcity

of money, and consequent shortage of medical personnel has prevented the complete Medical survey of the country. The exact geographical distribution of Schistosomiasis in the Sudan is therefore not yet definitely known.

Writing in 1904 Balfour¹³ said that Endemic Haematuria (Bilharzia) was of frequent occurrence in the Egyptian soldiery and was not supposed to exist in the Sudan save in such cases as had acquired infection in Egypt or elsewhere, but three Khartoum schoolboys (two of them brothers) had been sent to the laboratories and all three had shown blood and characteristic ova in the urine. They had all three drunk water from a school well, and all three had drunk from and bathed, in the Blue Nile. As a consequence all the school boys were examined (73 in number) and 17% were found to be infected.

In the same year cases of Bilharzia from Kassala Province, in Arabs who had not been to Egypt, were reported. "They may have visited Abyssinia."

Again, writing in 1908,¹⁴ he said "At present it is not much in evidence, save amongst those who have lived in Egypt."

In 1909¹⁵ it was reported in West Sennar (the present Blue Nile and Fung provinces) in enormous numbers. Although suspected to be present before that

date, in 1921 it was reported to be endemic in Dongala Province.¹⁶ Since the war which naturally prevented much actual research work the Medical Directorate have adopted a general progressive policy in regard to the detection, prophylaxis and treatment of Bilharzia and it has been reported in various places in the provinces of Kordofan, Darfur, Nuba Mountains and the White Nile Province."

Cases have been reported as far south as Mongalla.¹² There are no records as to it having been found to any extent in the Bahr-el-Ghazel province.

ECONOMIC IMPORTANCE OF BILHARZIA.

The economic importance of the incidence, prophylaxis and treatment of Schistosomiasis in a developing country like the Sudan, depending as it does largely on agriculture, cannot be over-estimated.

In such a large country where the population is about 6,000,000 only, it must be realised that the great obstacle to development is lack of labour. This is specially marked and seen in the difficulty which the Sudan Plantations Syndicate have in gathering sufficient labour in the Blue Nile Province to do the necessary work of cotton growing. They employ large numbers of Falatah, a travelling fanatical Mohammedan people from the West Coast.

Further the development of agriculture in the Sudan depends on adequate and, if possible, increasing supplies of water, this again is dependent on the opening up and developing of an increasing number of irrigation canals. These will of necessity radiate from the main water supply, which is the Nile and its tributaries, and as, as will be seen later, there are potential hosts in the Nile, spread of infection to them implies that a vicious circle is set up.

It will be seen that Bilharzia prophylaxis and eradication presents a very big problem for solution.

In Egypt, a country which is also largely dependent on agriculture and with similar difficulties in regard to water-supply, Ferguson¹⁷ stated that in 1910 more than 1,000 post-mortem examinations made by him at the Kasrel Aini Hospital in Cairo revealed the presence of the disease in 40% of Egyptian males between 5 and 60 years of age. Leiper¹⁸ found that at a village called Marg 49 out of 54 school children examined were affected. It has already been noted that Balfour found 17% of school children infected in the Sudan in Khartoum in 1904. In Dongola province¹⁹ 5,000 people (30% of population) were examined in 1927 and 9.7% were found to have schistosomiasis.

The incidence of the disease will be seen to be considerably less in the Sudan than in Egypt, but the

figures are hardly comparable as there is such a difference in the populations.

PURPOSE OF THESIS.

In 1925/26 the writer was in medical charge of the Nuba Mountains province and there had the opportunity, in the ordinary course of duty, of noting the incidence of Schistosomiasis among the peoples of that province. The endemic areas in that province are shown on the accompanying map.

The Nuba Mountains Province has a population of approximately 478,200 people and an approximate area of 31,300 sq. miles. As will be seen from the map it is bounded on the North and West by Kordofan province, on the East by the White Nile province by purely artificial boundaries. In the South, the Bahr el Ghazel, a tributary of the Nile, separates it from the Bahr el Ghazel province. The nearest point at which its territories approach to the Nile is at Kaka. There are no real or permanent offshoots of the Nile in its territories. As its name implies it is largely mountainous country. Most of its Eastern territory is un-explored and un-mapped. Owing to the limitations set up by the impassable nature of its country and the distances between water, the people are naturally concentrated in areas to the north, west, and south. It will be realised that the greater part

of the water supply is adventitious water. The people of the province differ markedly from the rest of the people in the Sudan. They are primitive, savage, warlike and ignorant, but very attached to their "gebels." Although they vary in districts they are generally a tall, well-developed race.

As part of a general scheme the Sudan Government are developing the growing of 'rain-cotton' in the province very successfully. Large areas are consequently under cultivation and as a consequence a large amount of labour is employed. In addition labour has to be obtained for the necessary work of repairing and developing of roads, transport of goods, building and other government work. They have at the same time to grow their own food-stuffs, otherwise they cannot live.

The presence and increasing incidence of a debilitating disease such as bilharzia with its potential powers of spread, makes it necessary that, if progress is to be maintained, its eradication is essential.

At TaIodi, the chief town, there were two schools for boys, one maintained by the central government, and one by the local authority. The average number of scholars attending at these schools during the period of observation were 90 and 35 respectively. The ages of the scholars attending at the government school ranged from 7 or 8 years to as high as 16 or 17

years. The local school consists of small children whose ages varied from 4 years to 7 years. The larger school drew its scholars from the whole of the surrounding district, the other from Taledi itself. The children from both schools attended monthly for medical examination.

In the present thesis it is proposed to give a resumé of our present knowledge of Schistosomiasis and compare essential points with the incidence, and treatment of cases which occurred, among these schoolchildren. At the same time it is proposed to discuss measures of eradication and prophylaxis against Schistosomiasis in the Sudan.

II. HISTORICAL OUTLINE.

As a result of his researches into Endemic Haematuria, which had long been prevalent in Egypt, Theodor Bilharz²⁰ discovered Distoma Haematobium (S. Haematobium) in the portal vein of a patient at the Kasr el Aini hospital at Cairo in 1851. Dr. Joseph Harley²¹ found them in a patient in Natal in 1864.

It was realised that the parasite probably had an intermediate host and Cobbold²² in 1870, Sorsine²³ (1874-85), Lortel and Vialleton²⁴ (1893-1894), and Loos²⁵ (1895) attempted to find an invertebrate host for Egyptian Bilharzia but failed. Similarly Harley (1871)⁵⁹ and other workers tried by many experiments to infect animals and were unsuccessful.

Loos²⁵ worked out the anatomy of S. Haematobium in 1895 but apparently, as proved later, there was some confusion in his description and he included some of the characters of S. Mansoni, particularly in reference to the testes and gut, in his account of S. Haematobium.

He formulated a theory that the life history of Bilharzia differed from that of other trematodes in that the miracidium, or ciliated embryos, emanated from ova passed directly through the skin. To account for the failure of other workers to find an intermediate host he said that the only known host of B. Haematobia was man himself. He therefore said the

disease was communicable from man to man.

In 1903²⁶ Manson found in a patient from the West Indies, who had never been to Egypt, ova having a lateral spine. Repeated examinations of the urine were negative and there was no history of haematuria. As endemic haematuria was absent in the West Indies he conjectured that these ova were probably from a distinct species of schistosomes.

Balfour, in 1906²⁷, working in Khartoum described an interesting experiment. Water, in a well from which infected persons had drunk, was examined and a tiny, active crustacean was seen. Six active Bilharzia embryos (miracidium) were placed in water along with three crustaceans and left overnight. In the morning one dead embryo was found and the other five had wholly disappeared, and the crustaceans remained alive and active. They, in fact, lived for nine more days. Owing to the difficulties involved in the examination of the crustaceans nothing further was done at this time.

On geographical and morphological grounds Sambon²⁸, in 1907, confirmed Manson's conjecture that lateral spined ova were a distinct species. Since that date many cases similar to that of Manson's have been reported from West Africa, South America and the West Indies.

Holcombe (1907)²⁹ and Da Silva (1908)³⁰ first

described the anatomical differences between the adult *S. Mansoni* and the adult *S. Haematobium*.

In 1908³¹ Loos severely criticised Sambon's views, and denied the existence of two types of schistosomes, and a bitter controversy arose.

Sir Armand Ruffer³² found calcified *Bilharzia* ova in the kidneys of mummies of the 20th dynasty (1250-1000 B.C.) in 1910. As Christopherson² said, "So little progress has the Egyptian people made since Pharaonic times that the cause of this wide spread and obvious disease, by no means microscopic, remained undiscovered until 1851."

In 1906³³ Montgomery in India had discovered *S. Indicum*, *S. Spindalis* and *S. Bomfordi* in horses, sheep and cattle.

From the above it will be seen that very little progress had been made since Bilharz' original discovery up to 1910.

It was otherwise in regard to Oriental Schistosomiasis. In 1904 Katsurado³⁴ first described *Schistosoma Japonicum* the cause of oriental *Bilharzia* disease. This is especially noteworthy because it is largely owing to Japanese workers that *Bilharzia* disease has been elucidated. Fujinami and Nakamura,³⁵ working with *S. Japonicum*, proved that infection definitely entered through the skin, in 1908. They first

found domestic animals infected, and then that if non-infected cattle, dogs and cats were immersed in streams, popularly reputed to be dangerous, infection resulted. In 1910 they confirmed these experiments, using mice, which are not found naturally infected, and found young parasites in the portal veins three days after immersion. That man can be infected in the same way was proved by Matsuura³⁶ in 1910, who placed his legs in infected water and after some time passed ova in his stools.

Miyagawa,³⁷ in 1911, repeated all these experiments and described the morphology of the young worms at the time of skin invasion. They had the characters of cercariae and an intermediate host was hypothecated. Miyairi and Suzuki³⁸ incriminated a freshwater mollusc as the intermediate host of *S. Japonicum* in 1913 and early in 1914 Ogata⁵⁵ gave a detailed, accurate description of the bifid-tailed cercariae (or larvae) of the worm.

These facts completely upset Loos' hypothesis and showed that schistosomes conformed in essentials to the life-cycle of other trematodes. In the same year (1914) Leiper and Atkinson,³⁹ who were on an expedition to the Yangtse valley and to Japan to investigate Bilharziasis, amplified these observations and demonstrated the life-history of the parasite in the freshwater snail known as *Katayama nosophora* Robson,

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a new species; furthermore they infected mice with the characteristic cercariae through the skin and later demonstrated the adult worms in the portal system of these mice. Our knowledge of the life history of *S. Japonicum* was thus completed. Since that date other observers have found other molluscs which act as intermediary hosts for *S. Japonicum* both in Japan and the Yangtse valley, as for example Faust⁴⁰ and others.

Because of the large incidence of Bilharzia in the Nile Valley (61%⁴¹ and a deathrate of 10%⁶⁰) and the consequent danger of spread of infection to the large number of troops, as that operating in Egypt, the War Office sent out a special mission to Egypt in 1915. The members of the mission were Leiper,⁴² J. G. Thomson and Cockin. In a very short time, after the commencement of work, the non-eyed, bifid-tailed cercariae, characteristic of the genus, was found in two different species of snails.

Leiper in the next year completely vindicated Manson's and Sambon's theory that two separate ^{species?} existed in man, and that one *S. Haematobium* presented distinctively morphological features, laid a terminal spined egg, and developed in a sinistral and spiralled freshwater snail (*Bullinus* sp. *contortus* and *dybonski*) and that the other, *S. Mansoni*, gave rise to a lateral spined egg and developed in a flat freshwater snail,

^Pplanorbi boissyi. He also experimentally infected animals both via the unbroken skin and via the alimentary tract. By this work the life history of all three types was now completed.

As a corollary to this, Leiper, in the same paper showed how prophylaxis and prevention of spread of the disease could be carried out especially in Egypt.

Although so much had been performed in elucidating the aetiology of the causal organisms of the disease, the treatment of Bilharzia was still unsatisfactory.

The efficacy of Emetine had been noted by Hutcheson⁴³ in cases of *S. Japonicum* in 1913. Manger⁴⁴ (1918), Diamantes⁴⁵ (1917), Bonne⁴⁶ (1919), and Erian⁴⁷ (1919), urged its use with *S. Haematobium*.

MacDonagh⁴⁸ had used Tartar Emetic in the Boer War, but did not publish his conclusions until 1915, and then, in a form which attached little importance to the discovery.

Christopherson⁴⁹, in 1918, as a result of work done at Khartoum Civil Hospital, placed the treatment upon a firm and scientific footing, and many later workers have confirmed his claim that in Antimony we have a certain cure for both forms of Egyptian schistosomiasis. Christopherson² (1919) has since laid claim that Antimony is both curative and prophylactic.

It has since been used successfully by Cawston⁵⁰ and Libby (1923)⁵¹ in cases of *S. Japonicum*.

In 1919, Fairley⁵² published the result of his elaboration of a Bordet-Gengou reaction (complement-fixation test) by which infections can be detected. This was a masterly piece of work, and, in 1920, was confirmed by Murray⁵³ and he related its uses. In the same year Cort⁵⁴ confirmed the investigations of Ogata⁵⁵ (vide supra) in connection with the cercariae of *S. Japonicum*.

Cawston⁵⁶ working in Natal in 1921 discovered infection in man caused by *S. Bovis*, a schistosome which had been discovered by Sonsine⁵⁷ in 1913 in cattle and sheep in Egypt, and later in Sicily, Sardinia and Nyasaland. This was a doubtful case but Reynaud and Leger⁵⁸ in the Congo in 1922 found cases of intestinal schistosomiasis where the ova resembled those of *S. Bovis*.

Much other work has been done by industrious investigators on the clinical aspects, prophylaxis, treatment and pathology of the disease and this will be referred to as necessary when these aspects of the disease are discussed.

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1. Introduction.

✓ Leiper's latest dictum 1918 R.A.M.C. Journal XXX No.3 235-60. Bilharz discovered the worm in 1851 which he named *Distoma Haematobium*, but which was re-named *Bilharzia* in honour of its discoverer by Cobbold. In 1858, Welland had created the genus *Schistosoma* for the worm *Distoma Haematobium* of Bilharz and Von Seibold. Leiper says that the generic name *Bilharzia* which conformed to the general views on nomenclature in those days should stand as a perpetuation of the name of the discoverer.

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III. AETIOLOGY AND PATHOGENESIS.

(1). The Parasites.

a. S. Haematobium - The male is white, cylindrical and eleven millimetres in length by one millimetre in breadth. It has an oral and ventral sucker (of which the latter is the larger) placed together. The dorsal lip of the oral sucker is longer than the ventral lip. The worm has a cylindrical appearance because of the ventral infolding of the sides of the body. The body would be flat if it were not for this. A gynaecophoric canal, in which the female can be partially enclosed, is formed by this infolding. The outer surface of the body is closely covered with small cuticular prominences, especially on the dorsal surface. There are delicate spines on the suckers, and the largest tuberculations are situated on the inner surface of the gynaecophoric canal. It has proctode ? four or five large testes.

The female is somewhat darker in colour than the male, is considerably longer, being 20 m.m. long by 0.25 m.m. broad, and is more filiform. Her anterior and posterior portions remain free while her middle portion is usually enclosed in the gynaecophoric canal of the male. Except on the suckers and towards the posterior end, where there are numerous papillae, her body is smooth. The genital openings of the sexes face each other, and are placed immediately posterior

to the ventral sucker.

The ovary in the female is situated in the posterior half of the body at the union of the caeca and the long uterus contains large numbers of terminal-spined ova. The yoke glands have a limited range in the posterior quarter of the body. vague.

The sexes live apart while young, but on reaching maturity the female enters the gynaecophoric canal of the male.

The alimentary canal commences at the oral sucker, in both sexes, and the ventral sucker or acetabulum is prehensile in function. The oesophagus presents two dilatations, and bifurcates just in front of the acetabulum to form two intestinal tubes, which again unite into a median tube. As they unite late a short caecum is formed. The excretory system consists of two longitudinal canals which open posteriorly and somewhat dorsally by the excretory pore.

b. S. Mansoni. - The male worms are smaller than those of S. Haematobium and are more grossly tuberculated. Its testes are smaller and are eight or nine in number. portion

The female of S. Mansoni is smaller than that of S. Haematobium. The ovary is situated in the anterior half of the body in front of the union of the intestinal caeca, and the short uterus contains only one late-

ral spined egg at a time. Fairly says that he has occasionally seen two or even three lateral spined eggs in the same worm. The yoke glands are distributed extensively over the posterior two-thirds of the body.

In both sexes the gut branches unite early forming a long caecum. In other respects these worms are similar to those of *S. Haematobium*.

c. *S. Japonicum*.— The parasite closely resembles in general structure *S. Haematobium*. The suckers are placed close together at the anterior extremity of the body, and the acetabulum or posterior sucker of the body is distinctly pedunculated and funnel-shaped. In both sexes the suckers and the ventral surface of the body are provided with minute spines. The distinctive characters are its smaller dimensions, the male being 9 to 12 m.m. in length by 0.5 m.m. in breadth, and the female 12 m.m. in length by 0.4 m.m. broad, and the larger size of the acetabulum compared with the oral sucker, both of which are relatively larger than those of *S. Haematobium*. Katsurada has reported both male and female forms up to 20 m.m. in length. In the male the integument is smooth and non-tuberculated, and the posterior part of the body is relatively wider in the male, the sides overlapping one another far more extensively than in *S. Haematobium*. The oesophagus is provided with two bulbs, and the bifurcation of the

alimentary canal takes place, as in *S. Mansoni*, at the level of the ventral sucker, but the union of the intestinal caeca is effected more posteriorly, the united gut occupying a quarter to one-fifth of the total body length. The excretory system consists of two longitudinal canals opening posteriorly and dorsally by the excretory pore.

The male has six to eight elliptically shaped testes situated dorsally to the acetabulum. The vasa efferentia join to form a common duct opening directly posterior to it. There is also a large seminal vesicle.

The female is considerably thinner than the male, and the ovary is situated in the middle of the body. The gut branches immediately behind it. The yoke glands, well-developed, extend almost to the posterior extremity. The uterus also is well-developed, and occupies the anterior portion of the body. It may contain 50 to 300 ripe ova.

(2) The Ovum.

a. *S. Haematobium* - The ova of *S. Haematobium* are oval or spindle-shaped, and each egg on an average measures about 0.16 m.m. in length by 0.06 m.m. in breadth. At one end of the ovum is a short, stout, and very definite spine. They are voided in the urine, as a rule, and sometimes in the faeces, of the vertebrate host, and generally contain a ciliated

miracidium which, in due course, escapes through the ruptured shell.

b. S. Mansoni - The ova are bluntly oval and have a lateral spine. Usually they are slightly shorter than those of S. Haematobium being about 0.15 m.m. long by 0.056 m.m. in diameter. These ova are passed out in the faeces and sometimes, though rarely, in the urine, and hatch out a ciliated miracidium.

c. S. Japonicum - The ovum of this species is 40 to 60 μ in length and 38 to 40 μ in breadth. It has no spine but, as Leiper has pointed out, it has what may pass for a rudimentary lateral in the form of a minute, and easily overlooked, papilla. This is like an excrescence, in a cup-like depression in the cell.

The ova are said to enlarge in their passage through the tissues, and may eventually reach a length of 90 μ . They are voided in the faeces of the definite host. Ciliated miracidia hatch out from them. Meleney and Faust hold that the wide differences recorded by various observers is due to the degree of maturity of the eggs measured.

(3) The free Embryo (Miracidium).

a. S. Haematobium. - The ovum is somewhat brownish in colour when found in fresh urine, and it usually contains a ciliated embryo (miracidium). The embryo may escape, in a short time, through a transverse rup-

ture in the shell. This rupture is produced by the absorption of water. After its escape from the shell the embryo swims about but soon perishes unless supplied with water.

If water is added freely to the urine the embryo not only escapes quicker from the shell, but also continues to live, swimming and moving about very actively, for not more than 36 hours.

The body of the little animal varies greatly in shape while it is swimming. When advancing it is, as a rule, long, tapering somewhat posteriorly and when it is stationary it assumes a spherical shape. The cilia which, except on the minute papillary beak, cover the entire body are its means of locomotion.

A primitive intestine may be seen running from the anterior papillae. Two unicellular salivary, or cephalic glands may be seen, with ducts opening into the mouth, on either side of this. The bulk of the embryo is occupied by a number of germ cells, the posterior part by excretory tubules connected with large flame cells. The nervous system is represented by an oval, irregular mass lying in the centre of the body. Leiper and Ashworth have observed that the cuticle of the miracidium is composed of a number of polygonal epithelial cells. The body is divided transversely into three zones united by six or seven longitudinal strands.

b. S. Mansoni- The embryo in this species is similar to that of S. Haematobium except that, according to Cort, the cephalic glands of the Miracidium are somewhat larger, in proportion to the body length, than is the case of the embryos of the other two species of human schistosomes.

c. S. Japonicum - The embryo of this species is also similar to that of S. Haematobium, but the same author says that the cephalic glands of this species are perceptibly smaller than those of S. Mansoni and S. Haematobium. The miracidium escapes through a longitudinal split in the shell, usually opposite the spine. It survives as a free-swimming body, in fresh water, for 60 to 72 hours. (Faust and Meleney).

(4) The Bilharzia Cercariae.

The Bilharzia cercariae belong to the furcocercous group of the distome trematodes.

No general
description.

Leiper has pointed out that there are four features which distinguish the cercariae of the trematodes which cause human schistosomiasis from the cercariae of other trematodes. These are:-

1. These cercariae have no pharynx.
2. They have forked tails.
3. They have no 'eye-spots.' (These are two minute collections of dark pigment located in the anterior third of the body on either side of the middle line between the suckers. They are a feature of cer-

tain other fork-tailed cercariae, but are absent in the schistosome variety).

4. They have two sets of glands communicating with the mouth, and lying on both sides of the posterior end of the body.

The excretory system consists of six flame-shaped cells in the body, and two in the anterior region of the tail. The cuticle of all fork-tailed cercariae is beset with minute spines.

The cercariae have two suckers on the body, anterior and ventral.

There are minor features which differentiate the cercariae of the species of bilharziae. Generally those of *S. Haematobium* are slightly larger (0.472 mm) than those of *S. Mansoni*. The prominence on lateral view, of the ventral sucker in the cercariae of *S. Mansoni* distinguishes them from those of *S. Haematobium* (Fairley and Bahr). The cercariae of *S. Japonicum* are smaller than those of *S. Haematobium* or *S. Mansoni* and are 0.25 m.m. in length and 0.04 m.m. in breadth. The body is covered with minute spines. The oral sucker which is greatly developed, occupies the anterior third of the body and, as in the other schistosome cercariae, has, at its free edge, a number of minute papillae. There are five pairs of cephalic, or salivary, mucin glands, and as they mature they change from basophilic to oxyphilic.

On reaching maturity the cercariae of all three species escape into the water from the invertebrate host. As Leiper says, "In Bilharzia as in all digenetic trematodes the terminal phase of development in the intermediate host is the cercariae, and this alone is the infective stage."

They vary in measurements owing to maturity, contractibility, differences in nutrition and intrinsic size variation.

The excretory system is of generic, not specific value. Faust believes that the essential differentiating features lie in the number and microchemical reactions of the secretory cells. He gives the following table for the identification of the cercariae:-

Schistosoma	S.Haematobium	S.Mansoni	S.Japonicum.
glands...	'2 pairs with large nuclei 'and granular acid proto- 'plasm. '3 pairs with 'basophilic 'protoplasm.	' 4 pairs.	' 5 pairs ' which change ' to ' 5 pairs.
Duct openings	'5 pairs	' 6 pairs	' 5 pairs.

(5) Life History of the Bilharzia worms.

a. Introductory.

The characteristic appearances and morphology of the different phases in the life of the worm having been described, it is now proposed to give a connected account, or history, of its whole life so as to show how, where, and in what order these different phases occur.

Until quite recently the extra-corporeal life of *S. Haematobium* or *S. Mansoni* was unknown except for its first stage of free-swimming ciliated embryo. This gap in our knowledge has been filled, however, by Leiper's very thorough work, in Egypt, in connection with these most important parasites. He showed, in 1916, that the miracidia of *S. Haematobium*, and of *S. Mansoni*, after escape from the egg enter a fresh-water snail; in the case of *S. Haematobium* a *Bullinus* (*B. Dybowskii*, *B. innesi*, *B. contortus*), in the case of *S. Mansoni*, *Planorbis boissyi*. These are small molluscs abounding in the irrigation canals of Egypt.

In the case of *S. Japonicum*, Mirairi and Suzuki, Leiper and Atkinson, and later Meleney and Faust, have shown that the miracidia from the eggs of this species enter fresh-water molluscs of the genus *Hemibia*, which are found in China and Japan. The first observations made in this connection were made in 1913, by the first named investigators.

b. Extra-Corporeal Life of S. Mansoni and S. Haematobium.

The ova are passed either in the urine or faeces, or both, of the vertebrate host. When the egg comes into contact with water, which is a fluid of lower osmotic pressure, its chitinous envelope first becomes distended and then ruptures. This frees the contained, active, ciliated miracidium. This ciliated embryo swims about rapidly in search of its particular intermediary host for a period of from 24 to 36 hours to which it is attracted by chemiotactic influence.

According to Lutz the miracidia, after penetrating the antennae of the mollusc, cast their cilia and become converted into a sporocyst, in the interior of which daughter sporocysts form. These latter migrate to the liver and hermaphrodite gland, where they multiply by transverse fission to such an extent that the entire liver becomes permeated with the long, delicate, transparent tube-like bodies. Fairley holds that the miracidium enters the snails by piercing the pulmonary chamber by means of its piercing papillae and makes its way to the digestive gland, (or liver) situated in the central whorl, and that, in this situation, the germinal cells of the embryo multiply rapidly, and become hollowed out into mother and daughter cysts (now known as sporocysts) which radiate throughout the glandular substance.

These sporocysts appear to absorb nutriment through their walls, as they have neither oral sucker nor alimentary canal. They are capable of travelling by wriggling movements.

Inside the sporocysts, numerous bifid-tailed cercariae are produced by a process of internal budding. In a period of four to six weeks the sporocysts rupture, and fully developed, active cercariae are discharged. These make their way through the body cavity of the intermediate host into the water.

Leiper has observed that they are discharged from the mollusc in 'puffs,' a number being periodically shot into the water, and that this discharge occurs quite independently of the passage of faeces by the snail.

The cercariae can remain alive in water for 36 to 48 hours, and in this limited period they must meet their definitive host or else perish.

c. Mode of infection of Vertebrate (or Definitive) host.

When opportunity occurs the now free-swimming cercariae penetrate the skin of some suitable vertebrate - man, mouse, rat, monkey - casting their tails in the passage. They bore their way through the tissue by means of papillae on the oral sucker and, possibly, by a chemical ferment.(Fairley). Not infrequently in man, as in experimentally infected monkeys, cercarial invasion is accompanied by intense skin

irritation.

Leiper considers they are attracted by the warmth of the body as only a "slight degree of penetration" of the skin took place when a dead mouse was immersed in infected water. This was in marked contrast to the readiness with which they penetrated the skin of a living animal.

The larvae reach the portal system by means of the blood vessels and, possibly, via the lymphatics as well, of the definitive host, and there develop, in a period of five or six weeks, into adults of both sexes, attaining sexual maturity. Terminal or lateral spined eggs are produced according to species.

d. Experimental infection.

To obtain these results in the laboratory, all that is necessary is to place the living experimental animal, or a part - tail, leg or body - of such animal, in the water in which cercariae have escaped from the snail, care being taken that the dose of cercariae is not too large, as in such a case the excessive invasion of the liver may prove rapidly fatal. Leiper, Fairley and other investigators have performed this experiment many times.

As molluscs are liable to invasion by a variety of miracidia, sporocysts and many species of trematode, it is necessary that cercariae experimented with should have the specific features of the cercariae of *S. Hae-*

matobium or *S. Manson*i. (vide supra).

e. Habitat in Definitive Host.

The males of *S. Haematobium* appear to leave the liver early and to make their way down into the finer branches of the mesenteric veins before they obtain maturity, and while the females found in the gynaecophoric canal ^{are} diminutive.

They occur in the portal, inferior mesenteric and mesenteric veins, but are in greatest numbers in the pelvic plexuses, the vesical and the uterine. Hence the worms may wander into the inferior vena cava, and may be actually filtered out into the lungs.

Their numbers vary considerably. As many as 300 may be found in the portal vein and its branches, and in experimentally infected monkeys there may be many more. Loos has seen the submucous tissue of the bladder so rich in worms that a pair could be found in every area of half-a-centimetre square.

The males of *S. Manson*i remain in the liver until the females (in copula) begin to lay eggs, and large numbers of lateral spined eggs are frequently deposited in the branches of the portal system. According to Fairley, their habitat, in infected monkeys, was the inferior and superior mesenteric veins and the portal system of the liver. Although the adults of *S. Manson*i were never found in the lungs its ova were.

f. Deposition of Ova in the tissues of Vertebrate host.

f. Deposition of Ova in the tissues of Vertebrate host.

The exact nature of this process, and also the method of exit of ova from the body have been studied by Fairley and Manson-Bahr from observations upon experimentally infected monkeys whose mesentery had been exposed under anaesthesia.

When the time for oviposition arrives the paired worms travel against the blood-stream to the furthest possible point. Here the female leaves the male partner, and being of smaller diameter, is able, by means of her suckers to progress until she stretches the smaller venules to the uttermost. The ova are then ejected with their spines directed posteriorly in front of the anterior sucker. The female then withdraws a little and repeats the process. As she withdraws the blood current tends to assume its normal course, the vessel wall contracts upon the ova, and thus forces them onwards engaging their spines in the vessel wall. The blood now forces the ova through the wall into the perivascular tissue. Fairley says that hereafter their progress through the tissues is independent of their spines and is brought about by an active ulcerative process. This Perry has denied and he has by microphotographs shown that progress still depends on the use of the spines.

g. Exit from body of Definitive host.

It would appear that ova, freshly deposited in

How?

this manner in the submucosa of the bladder, are voided in the urine only a few hours subsequently, and it is due to the rupture of these small blood vessels that the blood leaks out into the urine at the same time. The ova of both *S. Haematobium* and *S. Mansoni* may in like manner enter the faeces by passing through the intestinal wall. It is interesting to note that in experimentally infected monkeys the localising symptoms in the vesical form of schistosomiasis appear at least two weeks later than do the dysenteric symptoms in monkeys infected with *S. Mansoni*, and that, terminal spined ova may be found in the faeces of monkeys before their appearance in the urine.(Fairley).

h. *S. Japonicum* (Life cycle).

The life cycle is similar to that of *S. Haematobium* and that of *S. Mansoni* and the mode of infection is the same. The differences which will be noted are those characteristic of this species of schistosome.

i. Extra-corporeal life.

The ova are voided in the faeces of the vertebrate host and are carried to water, where the ciliated miracidium escapes. It survives as a free swimming body for a period of 36 to 72 hours. During this period it meets its intermediary host which is a freshwater snail.

The miracidium enters the snail by penetrating through the gill filaments, or by piercing the tissues of the head or foot and attaining the lymph sinuses.

On shedding its cilia it becomes a sporocyst.

In three weeks it becomes an elongated spinous sac containing secondary sporocysts.

Leiper has confirmed that the sporocysts of *S. Japonicum* are more delicate and elongated than are those of the other two species.

By the end of the sixth week the sporocysts have reached the lymph spaces between the liver and gonads, and here the mother sporocysts rupture and release the daughter sporocysts which contain the germ balls of the cercariae. Bifid-tailed cercariae are found in the sporocysts by the end of the seventh week. This final differentiation also takes place in the lymph spaces for the larval worms never break into the liver or gonadal tissue except by accident.

j. Infection of vertebrate host.

The cercariae escape when development is completed, and opportunity occurring, they penetrate the skin of some appropriate vertebrate host (man, cat, dog, mouse etc.) in which they attain sexual maturity.

k. Habitat in Definitive host.

The habitat of the adult worms is the smaller mesenteric vessels, especially those draining the large intestine. Immature examples may be present in the portal and splenic veins, also in the gastric veins and in the coats of the small intestine, and even in the coronary veins of the heart. In cattle, but not in man, they have been found occupying the

pulmonary artery.

Miyagawa and Takemoto conclude that the young forms migrate from the lungs to the liver through the pulmonary veins to the aorta and the mesenteric arteries into the capillaries of the stomach and intestine, from whence they reach the portal veins. This has been confirmed by Faust and Meleney, by experiments, who hold, however, that larvae in an advanced state of development from the lung cannot penetrate the stomach mucosa.

1. Deposition of ova in the vertebrate host.

Ova are probably deposited in exactly the same way as described for *S. Haematobium*. They are found chiefly in the walls of the intestine, the liver, pancreas and mesenteric glands. They may be found in the spleen and have also been found in the brain.

m. Exit from body.

They are extruded from the blood vessels like the ova of *S. Haematobium* and *S. Mansoni*. They are discharged in the faeces of the vertebrate host.

(6) The Intermediate Hosts.

1. The Parasites and their incriminated Carriers.

a. *S. Haematobium* - The intermediary hosts of *S. Haematobium* are fresh-water snails of the Genus *Bullinus*. These are sinistral and spiralled snails. The following species of this genus were described and implicated by Leiper in 1915 in Egypt, viz:- *Bullinus*

contortus, B.dybowski and B.innesi.

Becker showed that *Physopsis* Africans, a mollusc closely allied to *Bullinus*, was an intermediate host of *S. Haematobium* in 1916. Dr. Anne Porter, in South Africa, found the cercariae in *Limnea Natalensis* in 1920, but this would appear to be rare as the species also occurs in Egypt, and has not been implicated there, or in S. Africa, by other workers.

Cawston has described a snail in Zanzibar called *Isidora* (*Physopsis*) *Ovidea* Bt. recently as being a carrier. He says that this species may be distinct from *Isidora Africana* (Krauss) and not merely a variety.

Langeron and others in Tunis have described *Bullinus Brochii* as being the host in that district of *S. Haematobium*, and Dye, in Central Africa, has incriminated a snail called *Melania nodocincta* Dohrn.

In Portugal a snail called *Planorbis dufourii* has been found to be the carrier of *S. Haematobium* by Bettenourt and Da Silva and others.

b. S. Mansoni - For this species the intermediary hosts are fresh-water snails of the genus *Planorbis*. These are flat freshwater molluscs. Leiper, in 1915, showed that *P. Boissyi* was a carrier in Egypt. *P. Olivaceus* was demonstrated by Lutz to be the host for *S. Mansoni* in Brazil in 1917, and this same species of schistosome by Leiper, Lee and Khalil in Dutch Guinea in the year 1921.

Iturbe and Gonzalez in 1917 described *P. Guadelupensis* as the intermediary host in the West Indies and Venezuela. There is a possibility that *P. Olivaceus* and *P. Guadelupensis* are identical species. In Central Africa Dye has named *Planorbis* sp. near *Sudanicus* (Martens) as a host for *S. Mansoni*.

P. Centrimetalis has been described by Christopher-son and others as also an intermediary in Brazil.

c. *S. Japonicum* - Miyairi and Suzuki announced the experimental invasion of a dark grey, seven spiralled snail, with dextral opening, by miracidia, in 1913. Leiper and Atkinson confirmed this in 1914, and obtained cercariae from specimens of *Blanfordia nosophora*, the snail in question.

This intermediary host was first named *Katayama nosophora* by Robson in 1915, and was referred to the genus *Blandfordia* by Pilsbry, and to *Hemibia* by Annandale. Still more recently it has been recognised as synonymous with *Hemibia Japonica*.

In 1922 Suyemori found that *Blandfordia Formosa* acted as the intermediary host in Formosa. Meleney and Faust showed in 1923 that *Hemibia Hupensis* was the carrier in the Yangtse valley.

2. Distribution of the Intermediate Hosts.

It would appear therefore that the genus *Bullinus* and its allied species has a fairly wide range in Africa, Abyssinia, the Euphrates and South Europe.

The range of the genus *Planorbis* is wider still.

In Africa it has been found in Lower Egypt, along the White Nile into the Sudan, in Central Africa, and the Congo. It has been reported from Arabia. Various investigators have found it in Venezuela, Dutch Guinea, Brazil, Surinam, Porto Rico and in other places in the South American continent, and also in the West Indies.

The molluscs which act as the intermediary hosts to *S. Japonicum* have been found in China in five provinces. These are Hunan, Honan, Hupeh, Anhwei and Kiangsi. In Japan it is present in four provinces. These are Yamanashi, Hiroshima, Okayama and Saga.

It is also found in various islands in the Phillipines, and in Korea.

3. The Habitat of the Intermediate Hosts.

As a rule these snails make their habitat in stagnant, or slow-running water, or else in its neighbourhood. There are certain variations to this depending on the species.

Bullinus is found in the larger irrigation canals, the smaller irrigation channels, and in village ponds and "birkets." *Physopsis* and its allied species are mud and sewage snails, although they are also found in bathing pools. Both of these are African species of snails.

Planorbis varies slightly, according to the species, in regard to its habitat. *P. Guadelupensis* thrives and lives in the beds of rivers and in sluggish irrigation canals, whereas *P. Olivaceus* is found in

the rice fields of Dutch Guinea, and also in stagnant pools and mud, where there is much aquatic vegetation. *P. Boissyi* is found in the smaller irrigation channels only in Egypt.

The *Hemibia*, or *Oncomelania*, live close to the edge of clear relatively still, fresh water. They are most plentiful on the banks out of the water but within two feet of the water's edge. They are also found on the water grass stalks, in the water, a few inches above or below the surface, near the shore. It never occurs on the main canals but on the small, and especially the terminal, branches. The snails' constant absence from the rice fields is due to their height above water-level. This refers to the district round Soochow in China, but is not always the case in other parts of the Yangtse valley where the ricebed in which the rice is sown, is very often the source of infection.

In China *Katayama nosophora* occupies the coastal streams, but in Japan it inhabits the ditches of the rice-growing regions to a much greater extent than the rice fields.

4. The infected Snail.

Leiper has described how after obtaining entrance to the snail, the miracidia form sporocysts, which form daughter cysts and how these migrate to the digestive gland (or liver) of the snail and there grow rapidly.

He continues, "They become greatly elongated and eventually ramify throughout the organ, so increasing its bulk that an infected Planorbis can be detected at a glance. The colour also of the organ is changed. In Planorbis Boissyi the digestive gland is dark brown or black, but when infected this changes to ochre.... As the cercariae develop within them, the sporocysts may become markedly constricted by the host tissue.... The glandular tissue of an infected organ disappears apparently through pressure atrophy.... They (the cercariae) are discharged from the infected mollusc in "puffs," a number being periodically shot into the water. This discharge occurs quite independently of the passage of faeces by the snail."

Lampe has estimated that the discharge of cercariae from *P. Guadelupensis* is at the rate of over 2,500 per diem.

From observations on *P. Olivaceus*, Lutz has said that when the cercariae are developing from the sporocysts, in the liver and hermaphrodite gland, a state of very considerable marasmus is produced which proves fatal to the snail. The longest period that he was able to keep an infected snail was three months.

According to Fairley infected snails may be distinguished on macroscopic examination by the greater friability of the shell and by the change in colour it undergoes.

On placing such a snail in water, after a few

minutes, cercariae can be seen emerging with the naked eye or low power lens.

5. Seasonal Incidence of Infectivity.

From observation it would appear that the highest incidence of infectivity, for both species, in Egypt occurred in late autumn and December, although endemic areas are potentially infective throughout the whole year. This was shown as the result of 10,000 dissections of fresh water snails in Egypt by Fairley and Manson-Bahr. (Planorbis and Bullinus). (54% of P. Boissyi and 11% of Bullinus contortus dissected near Cairo).

In spring immature cercariae and sporocysts were the rule. It would also appear that S. Haematobium occurred in a much lower percentage of Bullinus than S. Mansoni in Planorbis.

There also appears to be a marked seasonal variation in the habits of Hemibia, for in cold weather it could not be found in localities where it had been abundant previously. Similarly immature forms have been found in the snails in the spring.

6. Factors in the infection of the snail.

According to Meleney and Faust the miracidia of S. Japonicum rise and maintain themselves within a few millimetres of the surface of the water. They are always in the upper stratum. Those of S. Haematobium distribute themselves evenly throughout the water and so will all snails in the vicinity. These phenomena are related to the habits of the intermediate host."

Although the host-parasite mechanism is based on a precise adjustment the miracidium is capable of a very wide accomodation as regards temperature and H-ion concentration."

The attraction of the mollusc for the miracidium is a chemiotactic phenomenon and lies in the mucous secretion.

7. Factors in the discharge of cercariae.

The temperature of the water controls the escape of cercariae from the molluscan host. The optimum temperature is 24⁰F. for *S. Japonicum*. Light and darkness have no effect on the discharge according to Isobe, neither has the character of the water, but Narabayashi holds that they are photophobic.

Working with *S. Mansoni* Mutz showed that 24⁰ to 30-31⁰C. was the optimum temperature and further he holds that they (the cercariae) are photophobic. On account of this he says that the most dangerous time for bathing is between 3 p.m. and 4 p.m.

8. Specific nature of Infection.

Leiper has shown that animals infected with cercariae from fresh-water snails of the genus *Bullinus* always produce adult worms which give rise to terminal spined eggs only, while those animals infected with cercariae from snails of the genus *planorbis* (as *planorbis boissyi*) give rise equally constantly to lateral spined eggs, and also that in no case do both varieties arise from the same intermediate host.

"Moreover, the adult worms reared from these two species show constant.... morphological differences."

Manson-Bahr and Fairley have confirmed the above observations for Egypt, and Miyairi and Suzuki and Leiper and Atkinson have proved that those animals (mice) infected with cercariae from *Hemibia Japonicum* give rise constantly to the eggs of *S. Japonicum*.

In certain instances these findings would not always seem to be strictly accurate, for in Portugal, (in which country no *Bullinus* snails have been found) the intermediate host of *S. Haematobium* is *Planorbis dufourii* (Graels), a snail which has also been known as *P. Cuneus* and *P. Metidjensis*. In the Congo district of Africa, as has been noted, *B. Contortus* transmits a rectal form of *S. Haematobium*. This may be due to *S. Bovis*.

Dr. Anne Porter has reported *Physopsis Africana* as having been found to harbour both *S. Haematobium* and *S. Mansoni*.

9. Recent classification of the Intermediate hosts.

Annandale regards the *Hemibiae* and *Katayamae* as mere sections of *Oncomelania*, distinguished by the fact that, the shells of the species included in the former have vertical ribs while those in the latter have not. He recognises five species, viz:-

1. Shell smooth, *O. Formosa*, *O. Nosophora*.

2. Shell with vertical ribs, *O. Sublaevis*,
O. Longiscata, *O. Hupensis*.

Of these *O. sublaevis* and *O. longiscata* are doubtful species, so that all the accepted species of *Oncomelania* are now known to be carriers of *S. Japonicum*.

In connection with the above, it has been noted, that the shells of the snails vary in size and density from one end of the Asiatic habitat to the other.

Those in the Upper Yangtse valley have the largest and hardest shell, while those from Japan are smaller and have the softest shells. There is a progressive gradation in specimens from intermediate localities. The slight markings on Japanese shells bear out the supposition that the two geographical species belong to the same genus.

According to Annandale also the three *Bullinus* (*B. Innesi*, *B. Dybowski* and *B. Contortus*) are specifically identical, and should be included in the species *B. Truncatus*. (*B. Truncatus* - Audouin, 1809, is identical with *B. Contortus* - Michaud, 1831).

10. Distribution of Intermediate hosts in the Sudan.

The distribution of the intermediate hosts in the Sudan has not been completely worked out for various reasons.

Leiper said, in reference to *P. Boissyi*, that it had an extremely limited range in Egypt but a wide range in the Sudan, and that it had been recorded on several points of the White Nile from Abba Island to

the Bahr el Zaraf. This was in 1916.

Archibald reported, in 1923, Isodora (Bullinus) Innesi, as the carrier for S. Haematobium, being present in quantity in Dongala Province.

The distribution at present would seem to be as follows:-

Province or District.	Endemic Carrier.
Blue Nile Province (including Gezira Irrigation and the Fung Province).	B.Contortus, B.Forskali, B.Pfeifferi and P.Alexandrinus.
Nuba Mountains Province.	B.Contortus, B.Forskali.
Kordofan.	B.Contortus, B.Dybowski.
White Nile Province.	P.Boissyi.
Mongalla Province (Yei River).	Physopsis Africana.
Dongalla Province.	B.Innesi.
Upper Nile Province.	P.Boissyi.

This supports the view, already mentioned that in districts not included in the Nile valley in the Sudan, the common type of Schistosomiasis found is due to S. Haematobium infection.

11. Breeding season.

Manson-Bahr and Fairley believe the breeding season of B. Bullinus to be the months of July and August. That of Planorbis is during April and May especially.

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(7) Pathology; Changes following Schistosome Infection.

a. Introductory.

The pathological changes due to schistosome vary greatly in character according to the degree, and, more especially, the duration of the infection. They also vary greatly according to the species of bilharzia with which the individual is infected.

Hutchison holds that bilharzia worms and ova in the tissues induce a primary inflammatory reaction of a non-suppurative nature, and that they have no inherent capacity to produce inflammation and further, that the latter seems to depend on secondary bacterial invaders acting on tissues of diminished vitality. Abscess formation has not been seen in the deeper tissues and in the abdominal organs. The ova are at first surrounded by inflammatory cells, and then become isolated by fibroblasts and giant cells of the foreign body type. Ultimately a granuloma forms, the characteristic unit of which is the Bilharzia pseudo-tubercle.

In Fairley's opinion the characteristic features consist of an infiltration of eosinophile and round mono-nuclear cells, and actual softening may form in the centre of the whitish nodes (or tubercles) which are analagous to the eosinophile abscesses in Trichiniasis.

He agrees with Hutchison that the type of cell



reaction may be regarded as a response to the mechanical irritation produced by a foreign body, and says that giant cell systems are commonly present in the vicinity of ova, and may actually form a plasmodial mass completely enveloping them. As a result of his experiments he considers that ova in the tissues, as well as adult worms in the veins, exert their influence by virtue rather of a toxic secretion than by any actual mechanical action, but, while Hutchison agrees that bilharzia worms produce nocuous substances, he thinks these substances are probably the result of simple protein splitting rather than toxin production.

The granulomatous tissue formed in the lesions described is ultimately replaced by fibrous tissue.

The distribution of the microscopic lesions in the body corresponds to the blood supply; for example, in the liver it is the peri-portal zone, in the hollow viscera the sub-peritoneal and sub-mucous coats. The cytological response to bilharzia toxins is the eosinophile cell.(Fairley).

The death of ova, as well as adult worms, in situ which is sometimes seen may be due to local tissue reaction and the systematic response.

Ferguson has shown that ova may be demonstrated by digesting the tissues with 2% caustic soda.

b. S. Haematobium.

As a rule in infection with this species of schistosome the bladder is first affected. Injected

small vessels in the mucosa and perhaps some very small vesicular or papular elevations of the mucous membrane may be all that it is possible to see macroscopically, but if these be examined microscopically ova will be found even in the smallest blood vessels.

Later there are found circular, thickened, whitish patches of inflammation (pseudo-tubercles), especially in the trigone. These are very dense and are granular on the surface. Manson has said that they present resistance if cut with a knife. Numerous ova are found in these tissues and it is evident that they are the result of changes caused by the numbers of ova present.

The ova are most numerous in the sub-mucosa, their numbers are less in the mucous membrane itself, and they are fewer still in the vesicular walls and the submucous coat.

They are generally in clumps, or they may be round an occluded blood vessel, and are in various stages of development, some being calcified and some fresh. The patches may present minute sloughs or may be covered with phosphates.

Minet has described the appearance of these patches by cystoscopic examination. He holds that they are small yellow granulations "absolutely typical of vesical bilharzia." He has likened them to grains of millet in appearance and says they consist of small prominences of normal mucosa surmounted by a yellow

cap. On the other hand he holds that the granulations which occur in tuberculosis of the bladder are pale yellow, hemispherical vesicles which lie on a flat background of inflamed mucosa, and he considers that the miliary tubercles of tuberculosis and the pseudo-tubercles of vesical Bilharziasis may be distinguished by these features.

Pfister has found in his investigations that ova may be found in any part of the genital system, prostate, spermatic cord, testes, epidydmus, urethral glands and in the seminal vesicles, and not only in the last named as used to be thought.

Ferguson has said that, in the female, the uterus and ovaries may be invaded by bilharzia ova in considerable numbers. On the other hand Gibson's opinion was that Bilharzia infection of the uterus was unknown, but he stated that he had found ova in the vulva, vagina, cervix uteri and the fallopian tubes.

It should be pointed out that Fairley, in the experiments previously mentioned, has found that on section the uterus may present, in the sub-mucous zone, the same whitish nodes, or pseudo tubercles, of miliary bilharziasis which have been already described.

In the more advanced stages of *S. Haematobium* infection the internal organs present still further changes. Massive polypoid excretions or formations, which may be ulcerated, may protrude from the mucous surface, which is dark red and congested, into the

bladder. The mucous membrane may also be covered with blood-stained mucus containing numerous ova.

The bladder wall may hypertrophy. Phosphatic stones or gravel may be found in the later stages either embedded in the inflamed walls or free in the cavity.

Very similar warty, papillary or polypoid growths may also occur at the vulva and these can only be distinguished from venereal warts microscopically. Deep ulcers may also be found, and these, having papillary growths at the edges, may simulate carcinoma.

Within the vagina itself the common lesion is sclerosis. The mucosa is thickened and has a "wet sand" appearance.

Ferguson holds that the ovaries may be so altered by chronic oophoritis that this form of infection persisting from infancy must be a cause of sterility in young married women.

The ureters may also be infected, and even at an early stage may suffer from hyperplasia, may be occluded with small stones, or from thickening.

Ibrahim Aly Bey has described cases of schistosomeiasis which resulted in cicatrization, stricture and finally obliteration of the ureters.

Dilatation of the pelvis, and atrophy of the parenchyma, of the kidney may follow infection of the ureters, and hydronephrosis, pyelitis, abscess of the kidney, and similar secondary infections may develop.

S. Haematobium infection may cause 'sandy patches' with ulceration in the intestine, but it does not produce papillomatous growths in this region.

Hyperplasia from bilharzia infection may also occur in the prostate, vesiculae seminalis and cervix uteri. This leads to the corresponding ova strewn discharges.

Smith and O'Farrel have described a case of enlarged and congested spleen in which terminal spined ova were found at the autopsy surrounded by eosinophile cells, but Day holds that enlargement of the spleen is generally transient in *S. Haematobium* infection.

Cases of bilharzial infection of the appendix were found by Mouchet, with terminal spined eggs, which were clumped together, forming miliary tubercles under the serous covering.

Tumours of schistosome origin have been found in the peritoneum and calcified terminal spined ova in the spinal cord. According to Ferguson, in such cases of spinal cord infection the calcified ova are surrounded by well marked signs of neuroglial hypertrophy, which are seen on microscopical examination.

The ova have in addition been found in the liver, in gall stones and in the heart and kidneys.

Fairley, working experimentally, has abundantly confirmed all the above findings, and has described the pathological conditions found in the internal

organs of infected monkeys. In these he has described the liver as becoming enlarged and congested, and studded with whitish tubercles, 0.5 to 2 m.m. in diameter, which he considers are in reality minute abscesses composed of eosinophile cells. In the sub-peritoneal and sub-mucous coats of the colon these tubercles have a diameter of 1 to 3 m.m. The papillomatous growths of the bladder may attain a height of 5 to 8 m.m. He has also found the lungs to be affected with a condition resembling miliary tuberculosis. Further, in these experiments he found paired worms in quantity in the liver, portal vein, mesenteric and more especially, in the pelvic veins, as well as in the inferior vena cava and pulmonary veins.

c. S. Mansoni.

According to Dew, Fairley, Lampe and others the ova of *S. Mansoni* are very widely distributed in the body. They may be found in the liver, pancreas, small intestine, colon, vermiform appendix, stomach, duodenum, retro-peritoneal tissue, lungs, kidneys, lymph glands, brain, spinal cord, heart and ovary, as well as the rectum and bladder. In all these situations they cause tissue changes both from the irritative reaction and from a toxin produced locally by the worm.

This is especially marked in the liver where the eggs of *S. Mansoni* may be found in great numbers. Infection by this species is generally associated with

enlargement of the spleen and the liver.

The surface of the large and congested liver shows the characteristic whitish nodules. In this organ a peculiar form of 'pipe-stem' cirrhosis develops. Day considers there are two different types of cirrhosis found in old-standing cases and gives an explanation of their causation. The ova wander in the liver tissue leaving a trail of destruction with subsequent inflammatory reaction. Giant cell formation occurs in the new connective tissue formed and the ova are completely calcified and in time the majority of them disappear.

The type of cirrhosis apparently depends on the number and the rate of deposition of the ova.

If, as is more usual, the numbers are small and the ova are deposited over a considerable period, the diffuse form of cirrhosis (multilobular) is set up; if they are very numerous, they accumulate round the portal veins, producing dense peri-portal ("pipe-stem") fibrosis.

Dye has found in post-mortem examinations enormous numbers of lateral spined ova in the liver, associated with great enlargement of that organ, and Fairley, while confirming this, has noted that deposits of black pigment granules may be found in interstitial and secretory cells of the liver. These latter are probably haematoidin pigment granules, and they have been found, to a much smaller extent, in

S. Haematobium infections in the same situations.

The spleen, as noted above, is generally enlarged and shows signs of peripheral inflammations. Day is of opinion that enlargement is progressive and lasting when it accompanies the hepatic lesions of *S. Mansoni*. A case of splenic enlargement has been reported by Hodson in infection by this species of schistosome where, on clinical examination during life, the spleen extended to four inches below the costal margin.

It has been concluded by Coleman that Egyptian Splenomegaly is a special feature of *S. Mansoni* infection, and the researches of Day and Dye would seem to confirm this.

In Manson's opinion the enlargement of the spleen is due to toxic absorption, and he has stated that ova are not generally found in it, but Fairley has found ova in the spleens of infected animals and, according to Coleman microscopical examination of the spleen in Splenomegaly, associated with *S. Mansoni* infection, always shows the presence of the ova of the species.

The changes in the colon are generally constant. Sometimes the sub-peritoneal coat may be studded with minute nodules, and sometimes various grades of inflammation of the intestinal submucosa may be manifested by congestion, increased mucoid secretion, minute ulceration and scattered bilharzial tubercles. These cell accumulations or nodules may also occur in the mesentery.

'Sandy patches' due to deposition of calcified ova may cover large areas of the intestinal surface. These may cause a choleraic diarrhoea during life.

The coats of the large intestine are, as a rule, hypertrophied, and the mucosa the seat of dark red, or brown, polypoid adenomata, which bleed easily. These growths may ulcerate and involve large areas of the mucous surface. Obstruction may even develop.

Experimentally Fairley never observed actual papilloma formation in monkeys.

The mesenteric and retro-peritoneal lymph glands may be enlarged and Risquez has reported that thousands of ova were found on microscopic section of abdominal glands made at post-mortem examinations.

During his investigations Lampe has found that in heavy infections with *S. Mansoni* alterations in the lung are common, and that these changes are difficult to distinguish macroscopically from miliary tuberculosis, and he has also described a condition of disseminated myocarditis caused by the eggs of this species of the parasite.

Fairley holds that macroscopic evidence of the disease in the lungs and in the bladder is rare in infection with *S. Mansoni*.

Other wide spread changes may be found in the body which are due to toxæmia.

d. *S. Japonicum*.

The local reaction after infection by the cerca-

riae of this species of schistosome shows oedema, congestion and leucocytic infiltration of the skin.

Haemorrhages are produced by the young worms in their passage through the lungs and later through the alimentary tract. The outstanding feature of this form of the disease is the great enlargement of the liver and the spleen. The former is hypertrophied and nodular from the formation and contraction of the fibrous tissue which is formed as a result of the infection.

Kyore and Murakawi maintain that the induration of the liver is the result of thrombosis formation, due in part, to the adhesions of the eggs to the walls of the branches of the portal vein, and in part, to sclerosis of Glisson's capsule and its ramifications. According to Faust and Meleney a general "pipe-stem" cirrhosis of the large and small branches of the portal vein occurs. Ingestion by 3% potash solution shows the fibrous tissue contains many ova.

The spleen varies greatly in size. It may be hugely hypertrophied and ova may be found in it. The enlargement may be due either to toxic absorption, to back pressure, or to the presence of ova, or may be due to all three.

Deposition of black pigment occurs in both the liver and the spleen.

The ascites which is commonly found in old-standing cases is probably due to portal stasis.

The appendices epiploicae are greatly thickened and may be matted together.

The mesenteric and retro-peritoneal glands are enlarged, and thrombosis of the larger mesenteric and portal veins are frequently seen in late cases.

Hypertrophy and thickening of the lower parts of the intestinal tract are generally noted. Papillomatous growths are found in the intestines and Faust and Meleney have offered an explanation of their origin. They consider that abscesses form round the eggs in the tissues. When these break outwards into the lumen of the gut, by small openings in the mucosa, the cavities become lined by proliferating epithelium. This proliferates more and more until papillomata are formed. This theory may also explain the formation of the polypoid growths which are found in *S. Mansoni* infections.

The necrosis of the parenchyma, and degeneration of the convoluted tubules, of the kidney, which is sometimes found, is considered by Faust and Meleney to be due to the absorption of toxins, and to be generally associated with massive infections of the liver.

Eggs may be found in the pancreas. The lung lesions are usually insignificant, and the bladder, as a rule, unaffected. In some cases ova have been found in the cortex of the brain, and in the pia mater.

Wide spread changes occur also, in the body, in this form of schistosomiasis as a result of the absorption of toxins.

(8) Observations among School Children at Talodi.

These school children at Talodi, Nuba Mountains Province, have been selected as a convenient example to illustrate the type of Bilharzia met with in a non-irrigated area of the Sudan, and also to illustrate the wide distribution of endemic foci in a province, which relies on adventitious and unconnected water supplies to give the necessary water which may be required, and which, apparently, has no permanent water-courses draining into the Nile. The province is, moreover, dependent to a large extent on the annual rainfall for replenishment of these water supplies.

The incidence of the disease among these children should not be taken as typical of the incidence of the disease among the people of this particular province. Comparatively large numbers of cases were actually seen and treated during various tours made round the districts of the province, and it is worthy of note that all, or nearly all, were found to be suffering from the same species of the disease which was found among these school children, namely, *S. Haematobium*.

Except for a few children of either pure or mixed Arab descent they were all of Nubawi origin, and therefore shy, of comparatively low intelligence and instilled with all the ignorance, apathy and superstition common to their kind.

The Nubawis have implicit faith in their native

"fikkis" (magicians or medicine men) and are prone to view the white man and his works with suspicion. It is therefore extremely difficult to get into their confidence. For these reasons, together with their fatalistic apathy in regard to their own personal welfare, sick people are rarely seen in the early stages of an illness. They are much more commonly seen when nearly in extremis.

Education tends to break down this diffidence and lack of confidence but, even so, for example, only two, out of the total number of cases of schistosomiasis found in these school children, actually reported sick to the hospital of their own accord.

As will be noted later these prejudices, being more accentuated among the uneducated people in the outlying villages, seriously interferes with the work of prophylaxis.

During the period of nine months in which these school children were under observation 17 cases of bilharzia were discovered. 16 of these were pure *S. Haematobium* infections, and one only was found to be a case of *S. Mansoni* infection.

This latter occurred in the local school among the younger children, and at the time of its occurrence it was a matter of some speculation as to how infection had been incurred, as before this case, and, it may be said, subsequently to it, all cases of schisto-

somiasis found in the Talodi district were due to *S. Haematobium*.

It was discovered later that the child had been to Ed Dueim in the White Nile Province some nine or ten months previously with his father, and it is presumed that the infection was incurred there.

In one case only, of the *S. Haematobium* infections, rectal symptoms were present and terminal spined ova were found in the faeces. Repeated examinations failed to reveal the presence of lateral spined ova in this case.

Whenever a case was discovered the name of the patient, and that of his father, was taken with a view to discovering possible endemic foci in the district. In every case the children infected were found to have been inhabitants of villages where bilharzia was known to be prevalent, or afterwards discovered. In none of the cases was infection found to have emanated from the Talodi Gebels (mountains) themselves, that is, only the one case mentioned above occurred among the smaller children in the local school.

Statistics regarding the age of onset of the disease or its monthly incidence were unreliable for various reasons and have therefore not been quoted. Some children would only attend the school for a month or two, and would then return to their villages. They might then return to the schools for another short

period. Others would commence attendance, perhaps at the age of 16, and others again at the age of 4 or 5 years.

✓ They were, on the whole healthy and well grown for their ages. The prevailing diseases amongst them were chronic malaria and dysenteric diarrhoea. This latter was due to various causes, but more often than not, was amoebic in origin. As a result of the malaria enlarged spleens were by no means uncommon, occurring approximately in about 20% of the total number of children.

The detected cases were treated for the disease, as will be described later, and kept under observation until such time as they were thought to be cured.

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Although these enlarged spleens, generally of malarial origin, are so extremely common, they appeared to have little effect on the after life of the children. It has been observed that as they grow older, except for a minority of cases, the spleens gradually grow normal in size.

Another interesting point is the apparent immunity these people have to malaria. If, say, 50 people from the Northern Sudan, taken from districts where malaria is known to occur, and 50 Nubawis are put together to work under the same conditions in a malarious Southern district, as the Nuba Mountains Province, 50% of the northern people will become ill with malaria and be incapacitated for work, whereas only about 5% of the Nubawis will become effected in the same way.

This apparent immunity to Malaria has been noticed among other Sudanese tribes also.

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IV. SYMPTOMATOLOGY AND DIAGNOSIS.

A. Symptomatology.

1. Introductory.

a. Clinically the course of the disease, in all the three different types, can be divided into three stages.

First, there is the toxaemic stage, occurring from three to ten weeks after infection, and then the second stage of localised schistosome infection which occurs much later. In the latter the localised symptoms supervene as, for example, bladder symptoms in the case of infection with *S. Haematobium*, and intestinal and abdominal symptoms in the case of infestation with *S. Mansoni* or *S. Japonicum*.

Finally there is the third or terminal stage, which may or may not occur. It usually occurs in individuals who are hyper-infected as a result of constant re-infection, and is most commonly seen in Egypt, China and Japan. Advanced and generalised pathological changes throughout the body of the infected individual are characteristic of this stage, producing anaemia, wasting and debility, and which may end, and frequently does, fatally.

b. The initial penetration of the skin by the cercariae causes an intense pruritus, which itches and tingles. This is partly mechanical in origin, and partly due to an irritating substance excreted by the larvae.

The erythema thus produced was regarded, in the case of *S. Japonicum*, by the Japanese as a skin disease called "Kabure." (Narayabayashi).

The same thing follows after infestation with the cercariae of the other two human schistosomes - *S. Mansoni* and *S. Haematobium*. (Walton Smith and others,

c. Under the heading "Toxaemic Stage" the symptoms of all three types will be described shortly as they occur in this stage, as they are so similar. The heading "Localised Disease" will include short descriptions of the 2nd and 3rd stages of the disease, as they occur with infection with each of the species, under the name of that species.

2. The Toxaemic Stage.

The toxaemic stage was not observed in any one of the series of cases which occurred among the Talodi schoolboys. This may have been due to the attitude adopted by the natives, reasons for which have been referred to, or because the patients had been infected some time before the commencement of their attendances at the schools.

That this stage undoubtedly does occur has been proved beyond dispute by a number of observers. Very accurate descriptions of this stage have been given by Edgar, Basset Smith, Miyagawi and Laning in *S. Japonicum* infections. A similar stage for *S. Mansoni* infestation has been described by Flu in Surinam, and by

Lawton, who worked among Australian troops in Cairo. Archibald in Khartoum has described febrile symptoms in connection with *S. Mansoni* without eosinophilia.

The analogy for *S. Haematobium* infection has been completed by Fairley and Lawton.

The former has shown, moreover, that toxæmic symptoms are not dependent on infection by one species of *Bilharzia* alone, for he found it to occur in mixed infections, which are so commonly seen along the Nile Valley, as well as in infection with a single variety of schistosome.

In *S. Japonicum*, Laning has described this stage of the disease. It was marked by a high afternoon temperature lasting from three to six weeks, a comparatively slow pulse rate, evanescent oedema and urticaria. Pain in the abdomen occurred, generally in the upper part. A spasmodic cough was present with evanescent areas of pulmonary dullness. The patients suffered from either diarrhoea or constipation. There was marked eosinophilia and often mental depression was observed.

In Lawton's series of cases of *S. Mansoni* infection, the general symptoms of this stage consisted of a resultant pyrexia, with slow pulse rate, urticaria, marked abdominal pain, especially over the descending colon and in the upper right quadrant, anorexia, rigors and pulmonary symptoms.

There was a pronounced leucocytosis and a high eosinophilia. Often the stool was normal, but diarrhoea, lasting from 12 to 48 hours was sometimes outstanding. The incubation period lasted from 4 to 6 weeks, and the temperature from 10 days to 8 weeks. Exaciation was marked.

Fairley has confirmed and amplified these symptoms, which Lawton originally described as occurring with *S. Mansoni* infection, and has found that they also occur in schistosome disease caused by *S. Haematobium*.

He classified his cases, for this stage, according to the presence of the outstanding phenomena, into three classes. These were:- a. those presenting symptoms of urticaria and prolonged pyrexia, b. those with urticaria and pyrexia of less than ten days duration and c. cases with urticaria alone.

The urticaria he described as being of the most intense type, causing a general oedema of the face and wheals on the trunk and limbs. It is sudden in appearance, remarkably transient and lasts, on and off, from one to ten days.

These symptoms are probably associated, certainly at the commencement, with invasion of the body by the cercariae of the species, and their migration into the tissues.

3. Localised Disease.

A latent period supervenes after the disappea-

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rance of the toxaemic stage, and this may last for an indefinite period, of from 6 weeks to $2\frac{1}{2}$ years, before the characteristic symptoms of localised schistosomiasis are seen, although ova may be found in the dejecta during the whole time.

Classification of the localised symptoms is usually made according to the site of the lesions found, and according to the species of the parasite. These symptoms are due to egg deposition, by the worms, and their extension in the tissues of the body. The terminal stage symptoms are probably due to tissue proliferation and repair. This is well illustrated in the cirrhoses of the liver seen in *S. Mansoni* and *S. Japonicum*.

a. Vesical Schistosomiasis. (*S. Haematobium*).

The following description of early vesical Schistosomiasis is based on records made of the 16 cases of pure *S. Haematobium* infection which were found among the Talodi school children during the period under review. Incidentally it may be said that vesical bilharziasis, caused by *S. Haematobium*, is the common type of schistosome disease found to occur in districts of the Sudan not contained in the Nile valley.

The symptoms vary within wide limits. Passage of blood at the end of micturition is the most characteristic symptom of the presence of the parasite in

the wall of the bladder. This may occur with or without a sense of urinary irritation. As a rule only the last few drops of urine contain blood, but sometimes the whole of the urine passed is blood tinged and occasionally clots have been noticed.

It should be especially noted that pain is not an essential, or necessarily, a prominent feature of the disease, and that ova and blood may be passed in the urine without the patient experiencing any trouble whatever. This was so in four of the cases observed.

In eleven of the cases the cardinal symptom was a burning, or scalding, urethral pain, (hence the native name of the disease "boule har," meaning hot urine), or a deepseated pain, perineal or referred to the penis, during the passage of urine. This was followed by a terminal haematuria, which was sometimes a constant feature, and sometimes of a most irregular nature in its occurrence.

The pain, when it occurred, was not always referred to one area. It was sometimes complained of as occurring in the perineum, the urethra, the suprapubic region or in the loins, and sometimes even in the small of the back.

Pain, or a feeling of oppression in the suprapubic region, was especially marked during distension of the bladder and was quite common. Urgency was a common complaint but frequency of micturition, although

it was noted, was not very commonly seen.

In one case rectal symptoms were present, with the passage of blood and mucus in the stools. Actually in this case the symptoms, with marked tenesmus, were so acute as to amount almost to a dysenteric attack. The patient's stool was being examined with a view to discovering the presence, or absence, of amoeba when the terminal spined ova were discovered. It should be observed, however, that dysenteric symptoms, associated with *S. Haematobium*, are not commonly found. O'Connor has observed that clinically the most severe dysenteric cases due to *Schistosoma* were associated with the species *S. Haematobium* in his experience obtained with the Expeditionary Force of the Sinai Peninsula.

This patient was discovered to be passing terminal spined ova in the urine, also.

It has been noted by Fairley that the ova of *S. Haematobium* may sometimes be found in the stools before their presence is noted in the urine, and various writers have commented on the comparative frequency of their occurrence in the faeces.

As already mentioned repeated microscopic examinations failed to reveal the presence of lateral-spined ova in the dejecta of the patient.

On digital examination of the rectum marked tenderness, and erosion of the rectal mucous membrane

was found above the prostate lobes.

It was not possible to carry out cystoscopic examinations as the necessary apparatus was not available, but the conditions to be found at this stage would probably consist of some congestion of the bladder mucosa and possibly the presence of white submucous nodules might be observed.

The urine sometimes showed macroscopic evidence of mucous and blood, and tests revealed the presence of albumin. Microscopical examination of the centrifugal deposits of the urine revealed the presence of the characteristic ova, associated with pus and red cells. The ova are passed in a vagarious manner and were sometimes not found. Investigators have remarked on the occasional finding of adult worms, in copulae, in the urine, but this phenomenon was not observed in any of the cases under review.

In one or two cases signs of cystitis were present and gave rise to a good deal of suffering.

The blood picture presented certain constant changes. In ten cases the average count was 9.045, thus revealing a moderate leucocytosis. There was a relative decrease of the polymorphs and an average eosinophilia of 9.5 per cent was found on making differential counts. Eosinophilia is most marked in the toxæmic stage, Lawton has noted 50%, and it thereafter gradually decreases.

No abnormality was noted in the red cells or haemaglobin, except that usually a slight secondary anaemia was present.

The third, or terminal stage of urinary schistosomiasis, which supervenes only in hyper-infected individuals, such as the Egyptian fellaheen, who are constantly exposed to re-infection, have naturally not been observed in the school children.

In the Egyptian such complications and sequelae as septic cystitis, Hydro- and Pyo-nephrosis, urinary calculi, vesical new growth and stricture of the ureters may be observed. There may be also hypertrophy, or contraction or even dilatation of the bladder.

The disease may attack the prostate and seminal vesicals causing spermatorrhoea, and ova may be found in the semen. Milton has pointed out the extreme frequency of urinary fistulae, seen commonly in the perineum and posterior surface of the scrotum, from schistosome disease of the urethra, which cause, among other symptoms, pain, disability and intense discomfort. In the male infiltration of the penile sheath may result in an elephantoid condition, with chordee and perhaps actual obstruction to the flow of urine.

Mention has already been made of the conditions which may supervene in the female genito-urinary tract, and these conditions will give rise to symptoms depending on their severity, extent and sites of origin.

Large numbers of ova, in the lung, as pointed out by Turner, may result in interstitial pneumonia developing. Infection of the spinal cord and brain substance accounts for epileptic and paralytic symptoms from which the patients suffered during life.

As Day first pointed out, in these late cases the blood picture differs, in certain respects, from that previously described.

There is a relative and absolute increase in the polymorph neutrophiles, with a corresponding decrease in the eosinophile elements, and the establishment of a severe secondary anaemia.

b. Intestinal Schistosomiasis.(S. Mansonii).

Only one of the series of cases was due to infection by S. Mansonii. Indeed, as previously noted, this type of infection is rare in the Sudan except along the Nile valley.

The outstanding symptom in this case was the emaciation present, which was very marked. There was some pain found on palpation of the liver and spleen, which were somewhat enlarged. Enquiry elicited the fact that the patient had suffered from intercurrent attacks of diarrhoea and occasionally from fever. Pruritus was present round the anus. While under observation the intestinal symptoms were fairly slight and consisted of a sense of rectal uneasiness, and occasional attacks of dysenteric diarrhoea, with the

passage of blood and mucus in the stools. Tenesmus was sometimes complained of, and sometimes intestinal colic was present. The duration of the individual attacks of diarrhoea was not constant but varied from two to five days. The stools, in the interim, were solid and showed abundant yellow mucus.

Microscopical examination of the stools showed the presence of lateral spined ova in the mucus. No ova were found in the urine.

Occasionally the stools were streaked with blood, but real clots were not observed macroscopically.

The blood on examination showed marked eosinophilia (12%) and a moderate leucocytosis. The red cells had markedly pale centres and the polymorphs were decreased in number.

Pulmonary symptoms were absent except for the morning cough which these natives usually have.

The third, or terminal stage.

The late symptoms of the disease were not seen in this comparatively early case..

In the Egyptian felaheen, massive pedunculated submucous tumours and subperitoneal infiltrations from the colon may form. The former by sloughing may give rise to extensive intestinal ulceration, with consequent passage of blood and severe diarrhoea.

These lesions are easily palapable, and actual intestinal stasis, or distension may take place.

Sometimes branching soft growths are to be felt inside the sphincter ani. They are apt to be mistaken for piles. These growths have been known to actually protrude from the anus, and have been observed with the naked eye.

Localised thickening of the transverse and pelvic colon may be felt on palpation through the abdominal walls.

Induration and fistulae, with their attendant symptoms, due to infiltration of the buttocks with ova are not uncommon.

A coarse "pipe-stem" periportal cirrhosis, already described, is not very commonly observed at autopsy, but a finer grade is also found. Ascites, and backward pressure symptoms, such as oedema of the extremities, failing heart and kidney symptoms may follow the portal stasis, when the cirrhosis is marked.

Egyptian splenomegaly with its symptoms of enormous enlargement of the spleen, wasting, debility and febrile disturbances is reputed to be, as already noted, a late manifestation of the disease.

Pneumonia, from ova deposition in the lung is an occasional complication.

The diarrhoea may be acute and choleraic in type and a fatal issue may result.

In addition to the symptoms and changes noted, marked toxic symptoms are present leading to great

emaciation, anaemia and debility, and making the sufferer a ready prey to intercurrent disease, and a possible fatal termination.

Symptoms
appendix

c. Asiatic Schistosomiasis. (Katayama disease-S. Japonicum).

This very short account of this type of the disease has been compiled from the descriptions given by various observers.

The stage of localised disease in this form of infection is associated with enlargement of the liver and spleen. The patient has generally a heavy feeling in the upper abdomen, and all the symptoms of toxæmia may be present and be well marked.

Great emaciation is common and is followed by loss of weight and there may be a slight degree of fever at some time during the day.

As the result of the intestinal changes dysenteric symptoms supervene alternating with periods of constipation. This dysenteric diarrhoea is associated with the passage of blood streaked mucus containing the characteristic ova in the stools. The period of duration of the attacks of diarrhoea varies a good deal. Tenesmus and straining at stool is very commonly present in the majority of cases.

The characteristic ova are revealed on microscopic examination of the stools.

Microscopically the blood picture shows marked

eosinophilia and some secondary anaemia. Faust and Meleney have recorded that the blood-serum globulin is twice as high as usual in this disease.

The third, or terminal stage may, or may not, supervene, and takes place in three to five years if frequent re-infection takes place. It is marked by cirrhosis of the liver. This organ and the spleen may sometimes increase enormously in size. Sometimes the liver is found to be shrunken on examination.

As a result of the progressive cirrhosis and enlargement of the liver and spleen, and also from toxic absorption, ascites, oedematous extremities, marked emaciation, increasing weakness and anaemia are very commonly seen. There is sometimes a little fever and the intestinal changes result in the passage of blood and mucus in the stools associated with diarrhoea.

Papillomatous growths, large and massive, may be palpated, and so also may be the thickening of the intestine sometimes found. Albumen in the urine, and other kidney symptoms may develop following secondary pathological changes in that organ.

Jacksonian fits and hemiplegia from the presence of ova in the brain cortex have been described.

Other general toxic symptoms may develop and the disease, when pronounced, proves fatal, sooner or later.

B. Diagnosis.

1. Introductory.

It is not usually difficult to diagnose schistosomiasis, for the presence of the characteristic ova in the dejecta is decisive and establishes the diagnosis. The ova are easily seen with a low power of the microscope and, it should be remembered that ova are passed vagariously and that, therefore, a single negative examination of the dejecta does not exclude the disease.

If the ova are few in number then difficulties may arise, as they will also if the ova have ceased altogether to come away from the parent worms.

Even if the ova, which are the most certain evidence of the previous presence of the parasite, are no longer being passed in the dejecta, the damage and the changes caused in the tissues remain and are generally permanent.

A large proportion of the cases met with are latent ones, that is to say, they do not present any of the more urgent symptoms. This is especially so in the case of *S. Mansoni* infestations.

2. *S. Haematobium.*

a. Microscopic examination of the urine.

In this form of infection if the glass containing the suspected sample of urine be held to the light, there will be seen floating about in the fluid minute

flocculi, or coiled up mucoid-looking threads. These will gradually sink to the bottom of the glass, together perhaps with some minute blood clots, if it be allowed to stand. If now some of this deposit be taken up with a pipette and microscopically examined it will be found to contain terminal spined ova, red blood corpuscles and some catarrhal products.

The ova can best be demonstrated by means of a centrifuge. If the deposits obtained after its use be examined under a low power of the microscope the ova will be easily found, if present, associated with pus and red cells.

Where the ova are few or absent and the diagnosis is open to doubt the patient should be told to empty his bladder. The last few drops of urine, forced out by straining, should then be caught on a watch glass. If these drops be now examined microscopically the ova, if present, will invariably be found.

When examination of the urine fails to reveal the presence of ova, if the surface of the bladder be scratched with a sound and the shreds of mucus, so obtained, be examined, then a few ova, calcified it may be, but presenting the characteristic spine, may perhaps be seen with the aid of the microscope.

b. Albuminuria as an aid to diagnosis.

The presence of albumen in the urine is a fairly constant symptom in *S. Haematobium* infection, and its presence, or absence, in the urine may be used as a

moderately accurate practical test in order to discover infected individuals among the population of, either an endemic area, or an area in which this form of schistosomiasis is suspected to exist. It was used in the monthly examinations of these 120 school children. and has also been used successfully on tour, when large numbers of natives in a suspected village required to be examined.

Job working among Senegalese troops, and Davies working among Northern Sudanese have referred to the practical value of the detection of this symptom. Cawston in S. Africa has pointed out that albuminuria often appears before ova are passed in the urine.

The method employed was as follows:- The individuals to be examined were taken, 15 to 20 at a time, and a specimen of urine was taken from each one. These specimens were placed in test tubes and were either held by those who had passed them, or placed in racks specially provided for the purpose. A little nitric acid was then poured into each specimen of urine, in rotation, by the investigator.

The presence of albumen in any specimen, as shown by the acid test, was always confirmed by application of the heat test and the addition of a little acetic acid.

If blood and mucus were observed macroscopically, in the urine of any individual, they were taken as

prima facie evidence of the presence of the disease and, in consequence, in such cases tests for albumen were not carried out.

It may be that, by this method of elimination, a few cases of schistosomiasis, in a large number of cases examined, were missed, on the other hand it has been found that with the presence of the worm there is always albuminuria. These tests for albumen were carried out very quickly and the saving in time and labour was considerable, because microscopical examination of the urine, for the presence of ova, in all the people of the area or village under examination, was avoided.

Any individuals who showed macroscopic evidence of blood and mucus in the urine, and those whose urine was positive for albumen, were put on one side in order that more detailed microscopical urinary (vide supra) and systematic clinical examinations could be carried out later. This was done so as to confirm the presence or absence of the disease.

c. Cystoscopic examination.

Within two months of infection, in the early stages of infection the cystoscope reveals a few scattered, grey, discrete elevations (pseudo-tubercles) in the trigone, around the ureteric orifices. Later haemorrhagic papules may appear in a congested mucosa. Much later in the course of the disease characteristic

"sandy patches" and papillomata may be distinguished.

d. Concurrent disease.

Owing to its distribution infection with *S. Haematobium* may occur concurrently with chyluria, with stone, with vesical tumour, with gonorrhoeal cystitis, and with pyelitis, as well as with prostatic disease. It should not be forgotten that it may be the causal origin, or the deciding factor in the production of stone, vesical tumour, pyelitis and prostatic disease as already mentioned. Care must therefore be taken in each particular case to isolate the special factors to which each particular resulting disease may be attributable. The presence of ova, even if calcified, would naturally be a deciding diagnostic factor.

For instance in chyluria, the presence of oil granules or globules or even microfilaria, in addition to blood, mucus and ova, would be noted. The finger blood taken at night would show microfilaria. A use of a sound will demonstrate the presence of stone. Gonorrhoeal cystitis will have a definite history of gonorrhoea given by the patient. In prostatic disease enlargement of the gland and the age of the patient will help diagnosis. Vesical tumour and pyelitis, which may be primary or, secondary to schistosomiasis, will reveal the causal factors in their origin only after systematic examination and observation.

In all these cases, and in the case of other

complications, the presence of ova, calcified or fresh, accompanied by eosinophilia, are strong presumptive evidence that schistosoma infection is their cause of origin.

3. S. Mansoni.

The characteristic ova are generally easy to find under the lower power of the microscope in the faeces. Two or three or more specimens should be examined before arriving at a negative diagnosis, as they may be very few in number. They may be located much more readily in the outer portion of a solid, scybalus than in a fluid motion, especially in the mucus passed with the stool. According to Bandi and Fairley the characteristic ova may also be found in the urine in about 50% of cases.

If a little fresh water be added to the specimen under examination the miracidia will be seen to leave the ruptured ova and wriggle violently across the microscopic field. As already mentioned the ova are extremely vagarious in their appearance and a large proportion of the infections are latent.

If, in the presence of rectal disease, S. Mansoni be suspected, one of the adenomatous growths may be removed by means of a forceps and examined for ova.

Sigmoidoscopic examination may reveal the pedunculated, adeno-papillomata situated in the upper portion of the rectum, but usually it is unnecessary as they

can be felt by digital examination, and may even be seen protruding as polypoid masses from the anus.

In heavily infected individuals localised thickenings of the large intestine, and intestinal growths due to *S. Mansoni* may be palpated through the abdominal wall. They are more generally situated in the transverse and pelvic colon than elsewhere.

4. Diagnostic tests applicable to both *S. Mansoni* and *S. Haematobium*.

1. Complement-fixation Test.

In order to detect latent cases, that is to say, cases which do not present any of the more urgent symptoms, of which, as noted, there is generally a high proportion, Fairley devised an ingenious complement-fixation test, by employing as antigen an extract of the livers of infested snails, (*Planorbis boissyi*). He utilised the method of complement fixation first described by Bordet and Gengou.

To prepare the antigen a number of livers containing the cercariae of *S. Mansoni* are macerated in absolute alcohol. This is then filtered and then evaporated by means of a Sprengels exhaust pump. A saline extract is then made of the dried residue and the anticomplementary dose estimated. The general technique employed is the same as for the quantitative Wassermann reaction in syphilis. The reaction is apparently a group one, in so far that an antigen prepared from the cercariae of *S. Mansoni* will give

positive results with *S. Haematobium* serum. It occurs in about 89% of early cases of the disease, and is specific for both urinary (*S. Haematobium*) and rectal (*S. Mansoni*) Schistosomiasis.

A positive result may be obtained in early infection before the appearance of ova in the dejecta. It is a more reliable test in the earlier stages than in the later stages of the disease.

Fairley has said that the value of the test is twofold, in that 1. it affords a means of diagnosis not only in latent bilharziasis, but also in very early stages of the disease prior to the onset of vesical or rectal symptoms, and 2. that it affords a therapeutic index to the effect of a given drug on Bilharzial worms.

He has also suggested that it would be of value in determining an "endemic index" of the disease.

This work was confirmed by Murray in S. Africa, who used antigen made from the livers of infected *Physopsis Africana*. His technique was Taylor's modification of the Wassermann test.

He also confirmed Fairley in saying that the test was specific and did not occur with syphilitic patients free from Bilharzia.

2. Intradermal Skin Test.

Fairley and Williams (E. Eleanor) working together have obtained an intradermal skin test for Schistosomiasis. They hold that the test is of diag-

nostic value only, and does not afford an indication of the success of a particular treatment. This was because two patients, who were regarded as cured both on serological and clinical grounds, gave positive reactions. The antigen used was derived from the dried powdered livers of snails infected with *Schistosoma Spinalis*. The reaction is characterised by a rapidly appearing large white wheal surrounded by a zone of erythema. Delayed actions occurred 3 to 24 hours after the initial injection and seven out of eight patients with *S. Haematobium* infection gave immediate reactions, and three others showed delayed responses.

5. *S. Japonicum*.

In endemic districts all cases of urticaria should be kept under observation for a prolonged period. This is especially necessary if an eosinophilia persists after the termination of the primary attack. During this period the stool should be continually examined for ova of *S. Japonicum*. This similarly holds good for any cases from endemic districts who show symptoms of chronic intestinal disturbance, associated with enlargement of the liver and spleen. As in the other human schistosome infections the presence of the ova is decisive and establishes the diagnosis.

The most accurate method of detecting the ova

is to wash the faeces and hatch out the miracidia.

A complement fixation test may be employed as in *S. Haematobium*. Sueyasu in 1917 produced an antigen from the bodies of the adult worms and obtained a positive complement deviation with the serum of an artificially infected horse. He used the blood of horses previously used for experiments by Narabayashi and Fujinami, and found that by using both aqueous and alcoholic extracts of the adult worms as antigen, a positive test was observed in the immune animal and a negative one in the non-immune animal.

Faust and Meleney have shown that the blood serum globulin is twice as high as usual in this form of the disease, and the "globulin precipitation test" and the "aldehyde Test" which were regarded as specific for Kala-azar were found strongly positive in many cases.

Meleney, in a separate communication, has emphasised the value of the "blood serum globulin precipitation test" especially in estimating the effect of treatment, as if the worm is absent or has disappeared the test becomes negative.

Skinner believes that liver tenderness, together with the type of temperature and the blood picture, should be enough to settle the diagnosis, even if search of the faecal mucus fails to demonstrate the characteristic eggs or any signs of parasites of other intestinal infections.

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V. TREATMENT AND PROGNOSIS.

A. Treatment.

Modern treatment resolves itself into the treatment of infected individuals with (1). Tartar emetic, or some other compound of antimony, (2). Emetine, (3). Other drugs, used either for the treatment of local lesions, or for the general treatment of the disease either without, or in conjunction with, antimony or emetine, and (4) in advanced cases, where necessary surgical interference, either in conjunction with, or without, the administration of the above-mentioned drugs.

The weight of opinion would seem to prove that tartar emetic has a specific action on the parasites, and is the drug of choice, while emetine comes second in importance, is not so effective and reliable, and is slower in its action. The other drugs used, apart from preparations of antimony, are purely subsidiary and are used in conjunction with antimony and emetine.

In the later or third stage of the disease no drug is specific, and whereas the parasitic worms are killed, the ravages due to their continued presence remain, and very often operative interference is necessary for the relief of distressing symptoms.

(1) Tartar emetic.

a. The treatment of schistosomiasis was unsa-

*Tonacemic St.
Treatment*

tisfactory until in 1917 Christopherson, working in Khartoum, placed the treatment on a firm and scientific basis. Over 80 cases of the disease were treated between May 1917 and May 1919, and all were cured who had complete courses of injections of Tartar Emetic intravenously, and as a result of examinations after two years it has been concluded that the results are permanent.

Taylor, Newnham, Day, Lasbrey and Coleman, Libby and Tootell, amongst others have since confirmed his claim that Antimonium Tartratum is an almost certain cure for schistosomiasis, in all its forms, provided that treatment is begun either in the incipient or secondary stages. In the third stage, especially where there is marked liver and splenic damage, it is not so successful.

Treatment should not be given to all cases indiscriminately for general debility from whatever cause, and serious cardiac and renal trouble contra-indicates its use. Caution has also to be observed in the treatment of elderly patients, or those in whom cirrhosis and jaundice is present.

Because the bulk of the cases of *S. Japonicum* come for help in the advanced stage, it has been said that very little help can be expected from Tartar emetic as a therapeutic agent in China. This is true, to a certain extent only for advanced cases in Egypt.

The results of treatment by the drug are controlled by observations upon the presence or absence of ova in the dejecta of the patients, and by the changes in the ova themselves. The amelioration of symptoms affected is also an important factor in judging the results of treatment.

It is not possible to determine exactly when enough antimony has been given, although Fairley has said that the Complement-fixation test, which he elaborated, serves also as a useful index of the effects of treatment. This may be true, and probably is, but it can only be used in centres where well equipped laboratories are available and is not practical when treating large numbers of patients in outlying districts of a country like the Sudan.

b. Christopherson's method of using Tartar Emetic.

The intravenous injections are given on alternate days over a period of fifteen to thirty days. One half grain of tartar emetic is the initial dose dissolved in 6 c.c. of sterile normal saline.

These injections are increased by half a grain on every other day up to a maximum of two and a half grains at a single sitting. In giving the larger doses the total amount injected at a time is made up to 10 c.c. with sterile saline.

The full dose is 30 grs. given in a period of 4 to 5 weeks and the $2\frac{1}{2}$ gr. doses are repeated until

this amount of the drug has been administered. A patient may be regarded as cured who, after a year shows no symptoms, that is to say, passes no live ova, has no haematuria or other symptoms of the disease.

Not more than 25 to 30 grs. should be given on one course and, if another course is necessary, some months should be allowed to elapse before commencing it.

The stock solution of tartar emetic is made up in a sterilised vaccine bottle, with a rubber cap, in a strength of $\frac{1}{2}$ gr. to 1 c.c. of distilled water, and for use this is diluted with 5 c.c. of sterile saline.

The reason for continuing the full course in spite of apparent cure and disappearance of the worm is that the number of worms is usually great and they differ in individual susceptibility to antimony. Many will be killed by less than the full amount of the course, but the more resistant will merely suffer a temporary reduction of their activities and will recover if treatment ceases too soon. The treatment has not "failed" if ova return when a full course has not been given. Day has agreed that the usual cause of failure is insufficient treatment.

c. Modifications of Christopherson's Method.

Low and Newnham in a series of cases found that a total of 20 to 30 grs. of antimony were sufficient to effect a cure, but they were also of opinion that

it should not be given oftener than twice a week, at first in $\frac{1}{2}$ gr. doses, and then increasing upwards, according to tolerance, to $2\frac{1}{2}$ grs. which they considered a safe maximum. They diluted the injections up to 60 c.c. of normal saline solution.

Day, and later Khalil, have both found that the drug is best given in a 6% solution, (1 gr. in 1 c.c. solution). This is practically a saturated solution and so provides a valuable safety provision, as too concentrated a solution cannot be used, and a small syringe and a small needle is all that is necessary to give 2 grs. After a study of over a thousand cases Day advocates an initial dose of 1 gr., a second of $1\frac{1}{2}$ grs. and a subsequent dosage of 2 grs. on alternate days. The total he suggests should be $22\frac{1}{2}$ grs. given over a period of 4 weeks.

Khalil gives intravenous injections thrice weekly and starts with graduated doses, .5 c.c., 1 c.c., 1.5 c.c. and 2 c.c. subsequently.

For children under 18 years, one grain for each year of age has been advised as being necessary. The initial dose is $\frac{1}{2}$ gr. rising gradually to a maximum of never more than $1\frac{1}{2}$ grs., with a total dosage of from 12 to 14 grs.

Cawston considers that the Potassium salt is the best, and is less toxic in saline than in distilled water. He holds that if the dose never exceeds

1½ grs., lack of toleration is rarely experienced.

Cases have been noted by various writers where permanent cure has apparently followed a dosage of 12 to 14 grs. in adults.

With *S. Japonicum* Tootell administered 0.5 c.c. of a 2% solution of tartar emetic intravenously and increased this by 0.5 c.c. daily until 5 c.c. was given. He found that cures took place after the administration of 17 injections in 38 days.

Meleney, Faust and Wassall gave 2 grammes (30 grs) over a period of two months, but considered that 1½ grammes is sufficient for moderate cases.

d. Action of Tartar Emetic.

The drug would appear to have a cumulative action on the adult worm. Christopherson believes that antimony potassium tartrate kills the adult worms in the portal veins and its tributaries, and sterilises the contents of the ova which have been deposited in the tissues rendering them harmless, and, that the first of these two effects takes place early in the course of the injections, viz. after 3 to 5 grs. have been injected. Day found that 2½ grs. antimony tartrate were sufficient to kill the ova in 9 days.

action
+ 71 -

Although the injection of antimony appears to check, it does not stop altogether the elimination of ova in the urine and faeces, which may and often does go on at intervals for a year or two years, after the

complete course of injections has been given.

Christopherson considers that enough antimony has only been given when all the ova passed are blackened, shrunken with shapeless interiors and are incapable of hatching out under any conditions. He agrees with Leiper's view that ova make their way through the tissues by means of a digestive fluid and, that if, and when, the secretive apparatus is paralysed, the ova are unable to proceed and disappear from the faeces and urine.

The drug appears in the blood stream as antimony tartrate when given intravenously, and Christopherson holds that it does not seem to be necessary therefore to introduce the complicated picture of antibodies and indirect action on the parasite. It appears to permeate the egg shell and kill the ciliated embryos within them. Day endorses this view.

That bilharzia eggs are permeable is shown by the fact that the use of formalin, as a deodorant in the examination of faeces, sterilises the bilharzia eggs whereas hookworms are unharmed.

An experiment has been described as follows by Christopherson. If one tenth of a c.c. of urine, laden with ova, is diluted with 6 c.c. of tap water at 130°F. the ova hatch out in from 5 to 10 minutes. If one grain of antimony tartrate is added before the hatching, about half of the ova hatch. The addition

of 2 grs. of antimony tartrate to the 1 c.c. just about stops the hatching process altogether.

From this, and other experiments, he concludes that the drug has a profound and direct specific effect on bilharziasis in all its stages.

In regard to this experiment Khalil has observed that it is impossible to be sure that what occurs in vitro also occurs in vivo. Faust has described similar experiments in vitro with *S. Japonicum*.

Franca who has studied the action and effects of antimony tartrate says that after tartar emetic treatment the eggs may have a normal outline but with a structureless embryo, or be very small (77-101 μ) yellowish and granular or shrivelled. These latter have developed completely but have been subsequently killed by the salt. He believes that small granular eggs are immature and prematurely deposited or aborted, owing to the action of the drug.

He therefore suggests that after treatment the measurement of the eggs passed (ovometry) is a useful indicator of the effectiveness of the drug and the success of the treatment, in *S. Haematobium*.

In *S. Mansoni* the ova disappears suddenly, the females contain only one or two ova and disappearance is complete.

It is thought that the appearance and alterations noticed in the ova, or their absence, coincides with the death of the adult worm.

e. Results of treatment by Tartar Emetic.

A rapid improvement in the condition of the urine is soon observed, generally all traces of blood disappear after the injection of 15 grains. According to Taylor as the results of treatment by the drug, there are rapid disappearance of blood and ova from the urine, mitigation or disappearance of the hypogastric and perineal pains on micturition, improvement in anaemia, gain in weight, and a quite striking improvement in general appearance, and a feeling of well-being.

Using the drug Cawston has found that-(a). after the second or third injection the patient notices that the burning sensation, frequency of micturition or pain in the bladder have all gone, (b). that at the end of ten days the patient notices no more blood in the urine and (c). that at the end of one month's treatment the symptoms are not likely to recur.

It should be noticed that occasionally depression and increased albuminuria may supervene at the end of the third week, and this render suspension of treatment desirable for a while.

The presence of numerous dead eggs and cells suggests further treatment. A month's freedom from living ova in the urine suggests all the parasites are dead.

With S. Japonicum, Libby has found that after ad-

ministration of 4 to 10 grains of tartar emetic all ova disappear from the stools. If the drug is to be at all effective it will be shown when 20 grains have been administered.

Faust, Meleney and Wassall found the eggs ceased to appear after an average of 22 days giving 2 grammes spread over two months, and that miracidia were hatched up to the 32nd day, after 1.32 grammes had been injected.

Comment has been made on a rise in the eosinophilia of the blood following after the injection of tartar emetic.

f. Disadvantages of the use of Antimony.

Although in competent hands the drug is not dangerous there are several points which should be noticed. Some people show intolerance of the drug, and there may be delayed effects 3 or 4 hours after injection consisting of rigors, generalised pains, rise in temperature, headache, severe vomiting and abdominal pain.

In giving intravenous injections a very little of the solutions escaping into the tissues will cause abscess formation and perhaps sloughing. It is therefore contra-indicated in fat people and small children whose veins are inconspicuous or very small. It has to be used with great caution where there is

advanced disease of the liver and spleen, or where renal or cardiac disease is present, and in elderly persons.

Sometimes, on giving it, cough and pharyngeal irritation may develop together with nausea and vomiting.

If given slowly, with the solution at a temperature not below blood heat, but few untoward effects are noted. Orientals would seem to be more tolerant of the drug than Europeans.

g. Other Antimony salts or compounds used.

Colloidal antimony. This has the advantage that it can be given intramuscularly but the doses are comparatively large ranging from 5 to 10 c.c.

Sodium Antimony Tartrate. This salt is quite as efficient as the potassium salt but is more expensive and less stable. The decomposed salt is toxic.

Bayer S.B.212. This is a complex salt of an organic antimonial acid used in 2% solution. A higher concentration than this is toxic. (Strength:- 1 c.c. contains .005 grammes of the salt). By its use much more antimony can be administered in a given time and it is excreted much more slowly. Its disadvantage is the bulk of the injection. It is useful for children and fat people intramuscularly.

Stibnal. Miyigawa has used this in S. Japonicum

When?

Purgative

Muscular P.

Quercy?

ny/

infections and he says it is quite as efficient as Tartar Emetic in that disease. He used it very successfully in cases which were not too advanced.

"Antimosan. (Heyden 661). Specht has used this drug and has had success in cases treated with it. It is said to have none of the unpleasant after-effects of Tartar Emetic. He says that a further study of the therapeutic value of antimosan in endemic areas, where material is more abundant, would be valuable. It has been reported to have a milder reaction than Tartar Emetic but that its cost is prohibitive for it to be employed on a large scale."

*Use of other
organic
preparations*

2. Emetine Hydrochloride.

The use of Emetine was apparently first noted by Hutcheson who treated cases of S. Japonicum with it in 1913. It was tried in 1915 by Boulliez who obtained no definite results, but later Diamantes, Collyno and Monziols, Erian and more recently Cawston have commented on its usefulness in the treatment of Schistosomiasis.

Judging by the literature there would appear to be no unanimity of opinion in regard to its use.

a. Methods of use.

Many methods of administering emetine have been used and suggested. Diamantes claimed that in the treatment of simple, non-septic haematuria, caused by

schistosomes, emetine intravenously in doses of 0.05 to 0.1 grammes per injection had a definite anthelmintic action, and Erian from his experience of cases, in which he had fifty recoveries as the result of its use, considers that it should be given in massive doses both for *S. Haematobium* and *S. Mansoni* infections.

Collynon and Monziols gave doses of 0.08 grammes daily for 10 days and claimed that by the 15th day the ova, the haematuria and pain on micturition had completely disappeared. Day (1921) found that Emetine proved effectual, but he asserted that large doses were needed up to $3\frac{1}{2}$ grains for each injection, and that because of its irritant action in the tissues it was better given intravenously.

Later he altered his procedure, and had good results in certain cases, by giving it in the same doses as Tartar Emetic. (vide supra). The initial dose was 1 grain, the maximum was 2 grs., and the total amount given by him was $22\frac{1}{2}$ grs. in 12 doses during a period of four weeks.

The dose given by Bonnet initially was $\frac{1}{3}$ of a gr., and he increased this dose every other day until at the 9th injection he injected $1\frac{1}{2}$ grains. He then gave $1\frac{1}{2}$ grs. on alternate days until 18 grs. in all were given. The patient complained of giddiness, but at the end of treatment the haematuria disappea-

red, and the eggs were degenerate and had fragmented shells. His opinion was that emetine administered intravenously was the best treatment for bilharziasis.

Christopherson's method was to give 15 to 20, one and a half grain doses during a period of 6 to 8 weeks. He considered it second in value to tartar emetic.

3 grains is the maximum dose according to Manson, $\frac{1}{2}$ grain being the initial dose and the total dosage being 15 to 20 grains. It is best given in the intravenous route, using a 3% solution in sterilised water, strength being 2 c.c. containing 1 grain of the salt.

Cawston has claimed cures in all cases of patients under 15 years of age who were able to tolerate a total of 12 to 15 grains of the drug in not more than 24 days, and he has expressed the opinion that not only the dosage but the length of treatment is important when it is being used.

b. Results of treatment by Emetine.

It was found by Day that at the end of the course living ova could still be seen, but these disappeared subsequently and on further examination five months later none were revealed, and this he concluded showed that emetine has a cumulative action, and that it kills both worms and ova.

It would appear therefore that emetine is slower,

*Faulkner
Emetine with 2m*

and not so certain in its action in the treatment of bilharzia disease as Tartar Emetic, and that the dosage used by the various observers and the opinion expressed by them on its use vary a great deal. It has also more serious disadvantages (*vide infra*), and while it is the drug which may be used when for different reasons tartar emetic is not indicated, its value as a curative agent is secondary to that of tartar emetic.

*vide Fander
Emet. M.
more effective
than T. E.*

c. Advantages of the use of Emetine.

It would appear to be the drug of preference in the treatment of cases of (a). young children, or fat people, or those with veins too small or inconspicuous for intravenous medication, as it can be administered intramuscularly, (b). intestinal schistosomiasis complicated by amoebiasis, (many such are met in Egypt), (c). people who are intolerant of antimony, and (d). those with advanced hepatic or renal disease.

Its value would appear to be in its anti-haemorrhagic action especially where, as noted, amoebic dysentery is a complication.

d. Disadvantages of the use of Emetine.

It should never be forgotten that emetine is a powerful cardiac depressant, especially as such large doses are required. Deaths have been reported from cardiac failure, while numbness, and heaviness of the limbs are often complained of, and peripheral neuritis is a common sequel to its use. In large doses

it may produce vomiting. Its cost is prohibitive as a routine treatment for outpatients, and this factor limits its efficacy as a prophylactic on a large scale.

Lee has pointed out that with *S. Japonicum* emetine is slower and less satisfactory than tartar emetic in the treatment of that disease.

It should not be given if Tartar emetic is also being given at the same time, nor should it be given if tachycardia, weakness of the limbs, or other signs of cardiac depression become manifest.

3. Other drugs used in Treatment.

These consist of drugs used for the general treatment of the disease, and of drugs used as local applications for local lesion.

a. General.

Gordon tried to find a drug to be given orally after a suggestion made by Leiper in 1925. For this purpose he gave Emetine peri-iodide, 1 grain thrice daily, powdered in milk, for 15 days and obtained the same results as he obtained with emetine given $\frac{1}{2}$ grain daily for 15 days.

Briscoe tried various forms of treatment, for example, iron, male fern, methylene blue and various urinary sedatives. Quinine appeared beneficial. Thymol, benzene and eusol have also been tried, by others. All these were valueless. Job tried neo-salvarsan and found it ineffectual.

Daily intravenous injections of calcium chloride have been given by Petzatakis, in a 10% solution and dosage of 0.5 to 1 gramme for 10 days, and then every second day for 10 doses. It was useless in advanced cases, but compares with emetine and tartar emetic, in other cases, in his opinion

b. Local.

Local applications are useful, given in conjunction with Tartar emetic or Emetine. Excessive catarrh of the bladder suggests washing out with weak boric acid, and internal administration of cubebs, copaiba, sandal-wood oil, salol, urotropine and so forth.

Salol, thymol, turpentine and similar drugs may be used for both intestinal and bladder symptoms.

4. Treatment in Advanced cases.

In advanced cases where drugs are of little or no avail the main treatment is surgical for the relief of symptoms.

Lasbrey and Coleman hold that patients with surgical complications should be given 6 injections of Tartar emetic prior to operation as the subsequent progress made is very rapid.

Stone and troublesome new growths should be removed by operation. In cases where distress was extreme Mackie and others have had good results from perineal cystotomy and drainage. Perineal fistulae must be dealt with on ordinary surgical principles.

Where there is hyperplasia in the vagina and cervix, scraping is the best treatment. In regard to advanced cases where rectal disease has supervened Dolbey and Fahmy have shown that although tartar emetic will destroy the ova of schistosoma, the papillomatous conditions set up and the distressing symptoms resulting therefrom continue. Complete and permanent cure is only obtained by excision of the whole tube of rectal mucus membrane.

5. Treatment adopted in the Talodi School children.

Each of the cases among these school boys was given a short course of intravenous tartar emetic injections up to a total dosage of 15 grains. The injections were given thrice weekly, the initial dose being a grain in 1 c.c., the second being 1 grain, and thereafter doses of $1\frac{1}{2}$ grains were administered until the total amount had been given. This course was quite successful in all except five of the cases. The symptoms, that is to say the presence of ova, the haematuria and the pain on micturition, disappeared, on an average, after the administration of 10 grains.

As mentioned above in five of the patients the symptoms of haematuria, and the passing of ova returned after the lapse of a week or two after the completion of the course, the urine in the interval having been negative on examination. These five were then given a course of emetine, by intramuscular injection,

in exactly the same dosage and over the same period as for the tartar emetic.

This was, in all the cases, quite successful, and at the end of the period under review the cure still seemed to be complete and there had been no recurrence of the disease in any one of these boys.

No untoward symptoms were noted except that in two of them abscesses formed round the site of intravenous injection. This happened probably because, owing to the smallness of the veins (one patient was five the other seven years of age), a small amount of the antimony solution had escaped into the tissues.

Usually a slight cough occurred after the tartar emetic injection but, to this, no importance was attached. The same phenomena has been noted to occur almost invariably after the intravenous injection of quinine given in the treatment of malaria. 2

The first injection was given in 5 c.c. of sterile saline, and thereafter the saline was gradually increased to a total of 10 c.c.

The emetine was diluted with an equal portion only of distilled water for the intramuscular injections.

b. The method of injection.

1. Tartar Emetic.

The antimony solution to be given was drawn into

the barrel of a 10 c.c. syringe, to which was attached a fine needle. Thereafter the necessary amount of sterile saline was drawn into the syringe also. The syringe was then tilted once or twice to thoroughly mix the contents. A trained orderly then gripped the arm of the patient just above the elbow, thus compressing the veins with his fingers. Iodine having been applied the needle of the syringe was inserted into either the median basilic or cephalic vein. A little blood having first been drawn into the syringe, to make sure the needle was properly in the vein, the resulting solution was then slowly injected, the orderly meanwhile gradually and carefully loosening his grip.

It has been found that by this method tourniquets of any description are unnecessary and, while the arm is held steady in the first place, secondly the loosening of the fingers does not cause any movement, which sometimes occurs when a tourniquet is loosened. The injection having been completed the needle was then withdrawn and iodine applied to the wound of entrance. The greatest care was taken to try and ensure that none of the solution was allowed to escape into the tissues. The same method was adopted with every intravenous injection given.

While in these few cases among children the patients were made to lie down after injection for a

short while, in other cases treated among adults this has been found not to be necessary.

2. Emetine hydrochloride.

This was always injected intramuscularly, either into the muscles of the upper arm, when the injection was small in amount, or into the buttock.

The site of injection having been selected, and painted with iodine, the solution of emetine to be injected was drawn into the syringe. The needle of the syringe was then plunged deeply into the muscle substance, the injection was slowly performed, and the needle was then withdrawn, and the site of the entrance wound was painted with iodine.

It should be noted that among these children a very careful watch was kept upon the cardiac condition for signs of depression while the course of emetine was being given.

c. The control of treatment.

The results of the treatment were controlled by observations made upon the ova in the dejecta of the patients. 30 to 60 c.c. of warm water were added daily to the freshly passed urinary deposits. If ova are left too long in alkaline urine they fail to hatch, care was therefore taken that the deposits examined were always freshly passed. The diluted solution having been made in a glass vessel the hatch-

ing of the ova was watched.

It was found that as the treatment progressed the ova took longer and longer to hatch, and that they were finally no longer passed. Any that were passed in the later stages of treatment were dark and shrivelled.

As already staged it was found that usually after about 10 grains of antimony had been injected, ova failed to pass and the haematuria cleared up.

In the case of the S. Mansoni infection, direct observations were made upon the stools passed.

B. PROGNOSIS.

Several factors have to be considered in venturing on a prognosis. There are first the longevity of the worm, second the degree of infection and thirdly treatment and the stage at which it was commenced. Christopherson has related a case in which the patient, a doctor well versed in the microscopical examination of urine, found in his urine living ova, which gave rise to miracidia, 28 years after infection. A case has been reported of a Canadian soldier, who contracted the disease in S. Africa in 1910, by Robertson. The man left S. Africa in that year and was still passing ova and blood in 1916.

From a study of 466 cases, infected during the S. African war, Harrison in 1913 concluded that

schistosomiasis was a much more prolonged disease than had been previously thought, and that the direct and indirect mortality among Europeans, removed from endemic areas, probably did not exceed one per cent. In five of the cases the disease had lasted 13 years, in 16 for 12 years and in 57 for 11 years.

With regard to the degree of infection the greater the number of worms infesting the body, the more severe and extensive is the disease they produce. This is well seen in Egypt and China where hyper-infection is so frequently met with.

The incidence of severe infections in a district increases pro rata with the endemic index of the disease in that district.

The introduction of intensive tartar emetic treatment has considerably improved the outlook for patients suffering from the disease. Lambrey and Coleman in reviewing a thousand cases, treated by them, found that the mortality was under a half per cent., and this included severe cases of schistosome disease. But, as pointed out already, while treatment is extremely successful in the first and second stages of the disease, the third stage is not nearly so amenable to treatment, and the prognosis is therefore not so good. This is particularly so among the hyperinfected peoples of China and Egypt, where large

numbers of cases come for help when it is too late. It is not being too pessimistic to say, that among the lower classes in China, that is, in the people in poor circumstances, *S. Japonicum* infection is a serious one, and when pronounced, proves fatal sooner or later. In that country the gravity of any case depends, amongst other things, on the degree of infection and the circumstances of the patient. Of 42 people found to be infected by *Koiki*, near Shushima, Japan, only 22 were not in good health.

The prognosis of *S. Mansoni* infection is very similar to that of *S. Haematobium* infection. In this form the disease is generally latent, and even large intestinal polypi may give rise to little or no inconvenience. Cases must be regarded seriously which have actual obstruction to the intestinal canal and cirrhotic changes in the liver.

In *S. Haematobium* infection the prognosis is practically that of chronic cystitis, depending on a remediable, and not in itself a fatal, cause. There may be much suffering, and as a consequence, anaemia and debility may be produced.

Villous and epitheliomatous growths in the bladder may be found, calculi may form and disease of the ureters and kidneys may ensue.

The presence of the parasite seems to in no way

inconvenience the patient in the milder forms of infection, and serious consequences do not necessarily follow. Attacks of haematuria occur from time to time whether the case is mild or severe, but as a rule the amount of blood lost is insignificant. In some cases the symptoms would seem to clear up of themselves or be absent for years at a time.(Harrison).

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6. Prophylaxis.

As Leiper very truly remarks the only mode of dealing successfully with Schistosomiasis, apart from treatment, is to prevent its spread to uninfected persons.

What is equally true is that the spread of the disease can be controlled if infection of the intermediate host is also prevented, since both the vertebrate, or definite host, and the invertebrate, or intermediary host, are equally necessary in the life history of the parasite.

The prophylaxis of the disease therefore includes all the measures which should be adopted in order to attain the above mentioned ideals.

The problem is always a difficult and complicated one to solve, and is not only one of public health, but involves also economic, political, religious, and racial questions.

The inhabitants of the countries where the disease is endemic are generally uneducated, ignorant, and suspicious, and measures instituted with a view to improving hygienic and sanitary conditions, need to be slowly and tactfully introduced.

Prophylaxis, in its application, may be divided up into (a) general prophylaxis, which includes not only the general application of pro-

phylactic principles, as they may be applied, on a large scale to prevent spread of the disease both to the vertebrate and invertebrate hosts, but also measures taken for the eradication of the disease among the infected communities of different countries, and (b) personal prophylaxis as applied to the individual.

a. General Prophylaxis.

The life history of the Bilharzia parasite has been described, and it has been shown that it includes two cycles, an a-sexual one, passed in the invertebrate host, and a sexual one, passed within the body of the vertebrate host. A description has also been given of the manner in which the Schistosome worm passes from one host to the other in order to carry on the species.

If the life cycle of the parasite be interrupted at any one of the four stages of its existence, it will perish. It is on this fact that prophylaxis is based. For instance, (1) By the use of Antimony the adult worm can be destroyed during the period of its evolution in the human host. This constitutes the therapeutic method of attack. (2) It may be destroyed during the period of its evolution in the intermediary host by using appropriate methods of snail destruction. (3) The application of sound principles of hygiene may be used to destroy the free-swimming cercariae, in

5 lines
p. 12

order to prevent infection passing from the snail to man. (4) The adoption of efficient and healthy sanitary methods will procure the death of the ovum in the faeces and the urine, and thus prevent infection passing from man to the snail.

Endeavour should be made to apply all four methods together wherever possible, because no one method, of the four mentioned, by itself, can be relied on to completely interrupt the life cycle of the worm.

Whatever means are adopted it is necessary, before applying them, to study the customs of the people, and the soil conditions, in order that efficient safeguards may be established against the spread of infection.

The methods mainly relied on are therapeutic attack on the adult worm in man by the use of antimony tartrate, and prophylactic destruction of the molluscan hosts. Methods levelled against the cercariae and miracidia of the parasite are also important, but these require educative and propaganda work for their success, and they are subsidiary to the medical treatment of patients and snail destruction methods.

1. Therapeutic attack on the Adult Worm.

In this method the great standby is the use of antimony and its compounds. Christopherson

has reiterated, time and again, his belief in the prophylactic use of Tartar Emetic, and it is apparent from results already obtained that his belief is justified. It acts both on the worm and the ova.

a. Action on the ova.

The lethal action of Antimony tartrate on the ova is remarkable. Day has stated that he found that $2\frac{1}{2}$ grains (total) antimony were sufficient to kill the ova in nine days, and that dead ova were passed in the urine for some time afterwards. He also found however, that if insufficient antimony had been administered to kill the worm, the live ova returned. A very small dose suffices to sterilise the deposited ova, an action which begins, according to Christopherson, with notable punctuality on the ninth day of injections. As already stated this action depends on the permeability of the Bilharzia ova to chemical poisons. The result is that, when the ova are sterilised, the source of infection of the snail is removed.

b. Action on the worm.

The quantity of antimony necessary to kill all the worms, in different individuals, is not constant. Small doses are sufficient to kill some broods, but others require as much as 25 to 30 grains before their existence is terminated.

Therefore, as already noted, it is advisable in all cases to give a complete course of 30 grains.

The experiments already mentioned would tend to prove that the action of antimony on the ova and worms is a direct one.

The patient is rendered less dangerous to the community even if he stops treatment before he is completely cured, for some of the worms will have been killed. The relief he experiences from the treatment will probably make him return for further injections, if the symptoms return ever so slightly.

It has already been stated that in almost all cases where a complete course of treatment has been administered, all the worms and ova are destroyed.

c. Advantages of Therapeutic Attack in Prophylaxis.

The great advantage of this method is that the relief of symptoms is so obvious that the native's innate suspicions are removed, and his co-operation ensured without effort. It will be readily understood that, without this co-operation, successful prophylaxis is impossible of attainment.

The effect of successful treatment with Antimony treatment in countries like Egypt and the Sudan, is that, as a rule, the natives are only too willing to give the method a trial, and to be injected and cured. There is no interference with religious

prejudices, long standing private habits, or economic practices. They are getting, in any case, something for nothing, and, provided the government of the country concerned is an enlightened one, and will provide the necessary facilities, the results are bound to be successful and gratifying.

Close contact is made with the native by using therapeutic treatment, and so many opportunities are obtained for propagating simple sanitary and hygienic truths, to the people directly concerned.

d. Where Therapeutic attack is Contra-indicated.

Therapeutic eradication of the adult parasite postulates the absence of a "reservoir" host. If reservoir hosts, apart from man, are present in a country, then it is useless to rely solely on this method only in order to secure complete eradication of Schistosomiasis. This is well illustrated in the case of Japan, where domestic and other animals, are heavily infested with the disease and act as "reservoirs".

In that country, cattle, horses, goats, pigs, cats, dogs, rats, and weasels, act as carriers of *S. Japonicum*, and are spontaneously invaded by the worm in nature.

Here-to-fore it has been thought that *S. Japonicum* alone had reservoir hosts among the primates other than man, and that the only vertebrate host of *S. Mansoni* and *S. Haematobium*, was man. This idea has been dispelled very recently by the researches of Cameron who has recorded the natural occurrence of *S. Mansoni* among the monkeys found on St. Kits in the Lesser Antilles.

Therefore in a country like Japan the main line of attack lies in wide-spread destruction of snails.

2. Prophylactic Destruction of the Intermediate Host.

Although a country like Japan relies mainly on snail destruction because the presence of reservoir hosts makes it useless to attempt to eradicate the disease solely by attempting to cure Schistosomiasis, the snail destruction should always be combined with therapeutic treatment. Patients are much more easy to find than are the snails. They are easier to cure, and a mollusc which is infected, remains so for months.

There are three main methods of procuring the destruction of the mollusc. These are (a) By dessication, contrived by controlling the water supplies, and the clearing of vegetation, likely

to harbour the snail, from potential breeding areas.

(b) By the employment of chemical poisons to destroy the snails. (c) By the employment of our knowledge of the bionomics and habits of the snail.

a. Methods as applied to Water.

Leiper in his valuable report on the Bilharzia problem in Egypt pointed out that in irrigated districts the precautions taken against snails depended on the government control of Nile water; that where irrigation was perennial, it was not always allowed to run; and that during the summer months, from April to August, the head regulators were periodically closed, a six days flow being followed by fifteen days cessation.

He found that Planorbis and Bullinus living in canals which had dried up during the fifteen days stoppage did not revive when placed in water. He therefore concluded that if the canals were correct in alignment so as not to allow puddles to form to act as a "carry over", this rotation itself would effectually kill the snail.

He also pointed out that the same object might be attained by the provision of an alternative route for the rotation water from the secondary canals to the fields. He further pointed out that chemicals could be added to the puddles.

Of prime importance is the constant removal of rushes, water-weeds, grass, and floating vegetation of any kind from the rivers or pools of the areas involved. Special attention should be paid to those places where there are natural obstructions in the water courses such as dams, sluices or fallen trees.

Wire gauze filters have been recommended to be used to restrain the movement of, and catch, the snail laden weed.

Snail destruction by rotation and control of water is not always successful. Blacklock and Thomson have shown that *Physopsis Africans* can survive for 14 days in mud in the shade, so that, cutting off the water has little effect on the human incidence of the disease in the endemic districts where these snails have their habitat.

The *Oncomelania* the intermediate hosts are operculate and so are resistant to drying or dessication. For these snails therefore other measures must be employed.

It should be noted also that, in Egypt, Khalil has said that the rise in subsoil water has spread *Bilharzia* by preventing the rapid drying of the canals when they have been emptied.

b. The Employment of Chemicals.

The Japanese have done much valuable work in this direction. The chemical employed should be lethal to the snail and, at the same time, should not be injurious to the crops. It should, furthermore act as a fertiliser to the soil.

Narabayashi has shown that lime is the most economical of the chemical agents in the destruction of the intermediary hosts of *S. Japonicum*. Unslaked lime is employed in a concentration of 1% for ditches and slowly moving water, and 0.1% where there are growing crops. It is the most efficient agent and is also useful as a fertiliser.

It has been found that rice fields in Japan heavily manured with human excrement, contain no molluscan hosts, although the irrigation channels are profusely inhabited by them.

Khalil, who has recommended the use of copper sulphate, has found that a dilution of one part of copper sulphate per million parts of rain water is lethal to the snails *Planorbis* and *Bullinus*, but when canal water was used as a diluent the highest dilution found lethal, was found to be 1 in 200,000, owing to the presence of humic acid and other organic substances.

He found that colloidal copper in a dilution of 1 in 4,000,000 was lethal to all molluscs in three days.

His experiments also showed that a dilution of one part of copper sulphate in one hundred thousand had no effect on the germination of cotton, maize or wheat.

Calcium cyanamide, calcium phosphate, ammonium sulphate, and chlorinated lime are also used and vary in their germicidal powers, fertilising properties and harmfulness to crops.

Cawston in S. Africa has recommended that miners' dams which have been found to be infected, should be treated with cyanide from the dumps, and he has stated that slaked lime is of even greater practical value than copper sulphate in shallow portions of large collections of water.

c. Use of Knowledge of the Bionomics of the Snail.

Atkins has recently shown that the distribution of snails is effected by the hydrogen ion concentration of the soil and water, which also effects the liberated miracidia.

Snails thrive best in neutral and slightly alkaline media. He writes, "it appears possible to kill organisms (which do not produce spores), the ever available source of the alkalies for this purpose being the mixtures of potassium and sodium

dilution

carbonates obtained by burning grass and vegetation!"

What did?

d. Factors militating against Snail Destruction.

The size of the endemic area is important. For instance, in China the intermediate host is spread over an area of 25,000 square miles. It is therefore useless to rely solely on snail destruction in such a large area. A very similar argument applies in the case of the Sudan. It is impossible to prevent the snails from becoming infected in such vast areas where the people practice promiscuous defaecation and urination, and where the people display such lack of knowledge, indifference, or apathy in regard to sanitation and hygiene. In large districts it is impossible, except by a very gradual process, to enforce sanitary regulations by police or other methods.

For instance, in Egypt, there are religious and long-standing agricultural practices. Snail destruction interferes with both, for the fellahs defaecate, and urinate, near water in order to use the water for ablutions as laid down in the Koran. The measures adopted in regard to irrigation and rotation of crops utilised in the destruction of the snail, are apt to interfere with old-established agricultural customs. The same trouble ensues in some parts of the Sudan, Dongola for example, where the natives are strict Mohammedans.

Another point to be remembered also is that the geographical distribution of the molluscan carrier is wider than the known endemic area of schistosomiasis.

3. Subsidiary measures of Prophylaxis.

These include measures to be employed for the destruction of living ova and miracidia, discharged from the vertebrate host, and the cercariae, discharged from the snail. They should always be used concomitantly with the other two main methods already described. They require education and propaganda work to ensure their success. The peasantry have to be awakened to an intelligent knowledge of the disease, and Day has recommended the use of posters and kinematograph films for this purpose in Egypt.

Water is absolutely essential to the schistosome outside the body, and therefore most of the subsidiary methods employed are concerned chiefly with the maintaining of a pure water supply, either by preventing it from being infected, or by killing the infective organisms contained in it.

It has been noted that if the ova are left without fresh water they die in a very short time. Similarly the free swimming embryo (miracidium) if it does not meet its appropriate intermediate host within 24 to 36 hours (in the case of *S. Japonicum* 36 to 72 hours), perishes also.

On discharge from the snail the cercariae cannot live more than from 36 to 48 hours, and will die also unless they meet their definitive host.

Full advantage is taken of these facts.

a. Miracidia and Ova Destruction.

To prevent their entry into water and so to prevent the infection of the snails is the first necessity, therefore measures should be taken to provide adequate latrine accommodation as far away from the water supplies as is possible. Promiscuous defaecation and urination near water should be prevented wherever possible, either by the enforcement of regulations, or by the gradual inculcation into the people concerned of sanitary principles.

Adequate and efficient measures of sewage disposal should be instituted to prevent water pollution.

In countries where faeces are used for manure they should be stored for three weeks before use in order to kill the miracidia.

Water supplies should be protected. The tops of wells should be raised and covered.

Reservoir hosts should be controlled, for instance, the keeping of cats and dogs should be prohibited, and horses used instead of oxen.

Exterminating measures should be taken against rodents such as rats, mice and weasels, who also act as carriers.

b. Destruction of Cercariae.

The people should be taught to avoid infected water. Mere dampness is adequate for the invasion of the skin.

All water should be stored for 48 hours before being issued to the consumer. Bore holes and water tanks should be instituted for the storage of water for drinking and washing purposes.

Leiper has shown that the Jewell system of filtration, as in the ordinary municipal filter bed, is ineffective in stopping the cercariae, for he found that the cercariae were active after penetrating 30 inches of sand, which they accomplished in five hours. He said the efficiency of such mechanical systems depends solely on the delay interposed "between the discharging mollusc and the consumer".

Shallow sand filters are also open to suspicion as cercariae succeeded in passing out, in large and increasing numbers, through four inches of desert sand after 15 minutes.

All water should be boiled before use, as this kills the cercariae.

Chemical agents may be employed such as ammonium sulphate, creosol (1 in 10,000), creolin, and lysol in water for bathing purposes and sodium sulphate (1 gramme tablet to the pint) should be used if necessary with drinking water.

Shallow ponds and surface water should be treated with germicides or drained. Snail-free watering and bathing places should be provided to prevent infection by the cercariae discharged by them.

Narabayashi has shown that the cercariae of *S. Japonicum* are killed by boiling the water, by drying, by a 10% salt solution, and by artificial gastric juice. He also pointed out that if the skin were coated with oil the cercariae failed to penetrate.

It is essential in drawing water for storage, in order to destroy the bilharzia cercariae, that no infective mollusc be admitted. This can be ensured by screening the intake pipe with gauze about 16 meshes to the linear inch. Ordinary mosquito gauze or phosphorus bronze wire is serviceable.

The surface of the water is most likely to be infected as the cercariae congregate there. An intake pipe should always be led therefore to the centre of the stream, and should draw the water from the bottom, at the place where there is little, or no, vegetation.

Ugi has shown that infective cercariae of *S. Japonicum* cannot infect the skin from a solution of 2% human excrement.

Lime solution (1 in 1,000) kills the cercariae in 30 minutes and has been recommended as a practical measure. It is therefore valuable both for the destruction of snails and cercariae. CaO?

Connor and Anderson have noted that soapy water is lethal to the miracidium, but Bettencourt has shown that although soap is lethal to the cercariae the salts precipitate the soap and render it inocuous. Hence the infection of the washerwoman at Tavira, in Portugal, is not hindered by the presence of soap in the water.

B. Personal Prophylaxis.

As infection can only be obtained by contact with water containing the cercariae of schistosomes, it is obvious that if the individual avoids contact with infected water, or water which is suspected to be infected, he will avoid infection with schistosomiasis. Therefore, in endemic districts, adults and children in particular, who are naturally the worst offenders in this respect, should be carefully and repeatedly warned against drinking, or bathing, in rivers, ponds and canals. Sportsmen especially, when engaged in snipe or duck shooting, and people who have occasion to wade in infected water, should wear long boots or water-proof waders.

Meleney has reported a case, which illustrates the necessity of wearing water-proof footwear in endemic areas, where infection occurred from wading about in ponds or pools, although the individual concerned wore shoes, socks, canvas puttees, and woollen trousers. Even fishing in freshwater canals in countries like Egypt is not free from risk.

Salt water swamps are safe.

All water, before being drunk, should be boiled or filtered, or have been previously treated with chemicals. A useful method (particularly for travellers in outlying districts of endemic areas, and soldiers who are often unable to obtain pure water supplies) is to use tabloids of sodium bisulphate, 16 grains (one tabloid) to a pint of water which equals a dilution of 1 in 567.

Chlorinated water (1 in 1,000,000) suitable for drinking, and which is commonly used in tropical countries has no apparent effect on the living cercariae. Fairley and Manson-Bahr found that four parts per million, and in this dilution water is unpotable, was not lethal to the cercariae in $2\frac{1}{2}$ hours. Recently Blackmore using chloramine solution, equal to one part per million of available chlorine, has found that cercariae were rendered immobile and in some cases showed evidence of disintegration in 30 minutes. The identity of

the cercariae was not proved by animal experiment although they were obtained from P. Boissyi, so perhaps these results are doubtful.

Bathing, or ablution water should be sterilised by creosol, lysol or creolin.

The individual should also be particularly instructed, whether he shows symptoms of the disease, or not, not to defaecate or urinate near water, in order to prevent the spread of the disease to others.

This is because it is known that a large proportion of the infected do not suffer from any trouble symptoms and are often unaware of infection.

C. Prophylaxis and the Sudan.

The Sudan provides an interesting illustration of the different methods which may be employed both in irrigated and in non-irrigated areas.

The country is so vast, and the nature of the country, the habits, religion, and customs of the people vary so greatly, that the problem is one which, for any given area, has to be solved separately.

The Gezira, in the Blue Nile Province, provides an illustration of an area where irrigation is under control, Dongola Province is an illustration of an irrigated area where, for various reasons, irrigation cannot be strictly controlled, and the

Nuba Mountains Province is an illustration of an area which is non-irrigated.

Water is supplied to the Gezira irrigated lands from the Blue Nile by means of the Sennar Dam, and to the irrigated areas in Dongola by the Nile. The Nuba Mountains Province is, except for a small portion on the extreme eastern boundary, dependent on adventitious water supplies.

1. The Gezira is an example of an area where, from the commencement of the irrigation scheme for cotton growing, scientific methods of approach to bilharzia prophylaxis have been put into effect with considerable success. In this scheme hundreds of square miles of land have been irrigated by water from the Blue Nile by the building of the Sennar Dam. The water obtained from this supplies a network of irrigation canals arising from larger main canals. This irrigation was also an example of the rapidity and ease with which the molluscan carriers can propagate and spread. Although this area was previously a waterless one, within about a year of the opening of the dam, and the consequent start of irrigation, Planorbis and Bullinus snails in quantity, albeit ^{not} infected, were found in the irrigation canals.

This supports the views of Leiper, Khalil,

and other writers, that artificial irrigation, which provides for the multiplication of molluscs, plays a great role in the spread of bilharzia.

By the energetic and active co-operation of the directorate of the cotton growing scheme and the Sudan Medical Service, the spread of the disease in this area has been controlled. Rotation of crops and water, with government control of the latter, efficient sanitation, examination and treatment (if infected) of the employees, clearing of vegetation and other methods of snail destruction and prophylaxis, are all practised with considerable success although, as will have been noted, four different species of intermediate hosts have been discovered, and the water is taken from a river which runs through the Fung Province and the Blue Nile Province, which are endemic areas of schistosomiasis.

2. Dongola Province consists of an irrigated and a non-irrigated area where in the scheme of irrigation, rotation of crops and of the water supply is not practised. Moreover it is inhabited by a fanatical type of mohammedan native whose main occupation is agriculture. We have here an example of a district where religious prejudices, deeply rooted insanitary practices, and oldstanding agricultural customs complicate the prophylactic

picture. The water supply is furthermore, mainly obtained from the Nile, which, as Christopherson has said in regard to its supply of snails, is "inexhaustible". Davies described the province as an unimportant one, but one which is a very important source of intelligent labour. He examined 5,000 natives (over 30% of the total population) and found 9.7% to be infected with schistosomes.

Archibald, who found large numbers of *Isodora* (*Bullinus*) *Innesi* in the irrigation canals, said that the measures for the eradication of the disease consisted of (a) action of anthelmintic drugs given to the infected persons, and (b) destruction of the molluscan intermediaries. He stated that method (a) could only be considered an incomplete one for eradicating the infection, on account of the number of infected women and children who would not submit to treatment, the difficulty of controlling the antimony therapy, and the existence of latent cases of infection.

He said that, although at first it would be difficult, the eradication of molluscs by interrupting the flow of water in the irrigation canals was a practical proposition. He recommended also the use of well water for ablution and drinking as a reliable prophylactic measure.

Smith, during tours of inspection in the same province, administered 10,000 injections of tartar emetic to 740 cases of urinary bilharziasis. Of these, 520 were examined up to $2\frac{1}{2}$ years after treatment, and 5.4% were still found to be infected. Only 3.5% of those who received a full course were infected at the time of writing.

It will be seen therefore that even with the many disadvantages which have been enumerated, much may be accomplished by prophylactic treatment in an area such as this.

3. The Nuba Mountains Province is, as has been stated, dependent largely on adventitious and unconnected water supplies. The inhabitants are, as has also been described, typical of the natives of bilharzia stricken countries, and are uneducated and ignorant and superstitious. They urinate and defaecate promiscuously all over the country side, but not necessarily near water, for the mohammedan population is small.

*much of
more before
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All the factors favourable for endemicity and spread are present, namely a warm climate, heavy, but not continuous, rains, abundant and wild vegetation, bad conservancy methods (in the native villages) and the natives wade in, and drink of, the available water in an indiscriminate manner.

The water supplies, which are abundant during the rainy season gradually dry up in the dry season, and consist in that season, mainly of "foulahs", "birkets", or "khors". That is to say, the water is mainly obtained from surface water contained in ponds, ditches, and shallow wells. On these both man and animals depend.

The snail, propagating its species in the summer season, is spread all over the country by the heavy rains and naturally accumulates in these scattered watering places in the dry season, the infected native is present and so the vicious circle is carried on.

The scattered nature of the infection in the province is well shown by the accompanying map. There are monkeys and baboons present in the province, also, and it may be, that these assist in the spread of the disease.

That all areas are not equally infected is obvious also from a study of the map, but whether this is due to the absence of the intermediary host, or to the fact that the different tribes of natives do not inter-mingle to any extent, is not known.

17 cases of schistosomiasis have been mentioned, 16 occurring in the larger government run "kuttab" or school, and one in the smaller "khalwa" (school) which was only government aided, and which contained

the smaller children who hailed from Talodi itself.

An analysis of these 17 cases shows the scattered nature of the infection also. Of these cases one was a case of S. Mansoni infection and the patient probably obtained his infection in the White Nile Province at Ed Dueim, which has already been referred to as an endemic area for schistosomiasis in the Sudan.

This was the only case which occurred among the smaller children.

Of the other 16 cases, 10 came from the Kawahla district, three from the vicinity of Gebel Fungor, two from Eliri, and one from Kadugli, all of which places, it will be seen from the map, are bilharzia infected districts.

None of the cases actually came from Talodi itself, and it may be mentioned incidentally, that apart from these schools, no adults found to be infected in the province, up to that time, were ever traced to have caught their initial infection there.

This was probably because the water supplies in Talodi were obtained from two government controlled, deep wells, which were well protected and locked up when not in use. In addition efficient sanitary arrangements, and methods of sewage disposal were enforced.

Although not found, it is inconveivable that the intermediary hosts were not present in the neighbourhood.

This illustrates the fact that, even if infection is present in a district, if efficient arrangements together with a pure and protected water supply are arranged for, the spread of the disease will be prevented.

It has been shown that the disease, as found, is amenable to treatment but, in large districts, such as the Nuba Mountains Province, only half-developed, with a wild and rocky terrain, and with poor roads, it will be easily understood that it is not feasible to procure successful destruction of the elusive intermediary hosts.

The methods of approaching the prophylactic problem, therefore, in an endemic area such as this, would seem to be (a) therapeutic treatment of the infected individual, and (b) the gradual provision of pure and protected water supplies. For (a) travelling hospitals, with a trained staff able, by reason of their mobility, to reach the infected villages, treat the infected people therein, and spread educational and sanitary propaganda, would be efficient, and for (b) the gradual provision, and sinking of, deep wells the filling in, or treating by chemicals, of the isolated ponds and ditches would seem to be the solution.

It is realised that it would not be always feasible or possible to find sites where wells, able to provide sufficient water, could be sunk in all the infected districts.

In these districts attempts should be made to clear the vegetation, and train the banks of the available surface water supplies, and methods of therapeutic attack should be concentrated upon.

It will be long before efficient sanitation, and cleanly habits in regard to defaecation and urination, although they are ideals to be propagated and hoped for, will be adopted by the ignorant and savage peoples of this province, and their racial suspicions, apathy and superstitions will provide many disappointments for workers amongst them. Much difficulty will be experienced too in getting some, especially the women and children, to submit to treatment, and, having submitted, to complete the course of antimony injections.

7. Conclusion.

It will be evident therefore, from a perusal of the foregoing thesis, that, in the light of our present and accumulated knowledge, the future prospect in regard to this disease, and its effects on the human race, is not one to be despaired of. In spite of the wide spread endemicity of Schistosomiasis in the world, and the profound pathological changes it causes in the bodies of the hyper-infected individuals, the researches of many illustrious and industrious investigators, into the problems it presents, are gradually bearing fruit. And these results are seen in many aspects of the disease, both in respect to its aetiology and pathogenesis, and to its treatment and prophylaxis.

Whereas in many areas, such as China, progress, from a variety of causes, political and otherwise, is slow of necessity, the outlook in other countries, such as Egypt, the Sudan, and Japan, is looming brighter.

While the study of the bionomics of the Schistosome and snail has considerably enhanced the spread and success of prophylactic doctrines, in Antimony we would seem to have a specific for the disease.

Many problems remain yet to be investigated in regard to this disease, as, for instance, the elucidation of the exact course of the worm, from the time of its initial entrance until it reaches its final habitat, in the human host, and the finding of a compound of antimony, or a substitute, which has not the therapeutical and practical disadvantages connected with the salts of Antimony in use at present.

Summary.

1. A resumé has been written, in the light of our present and accumulated knowledge, and based on the works and the conclusions arrived at by the many original investigators, of the three different types of human Schistosomiasis found in the world.

2. Various aspects in regard to the history, the distribution and incidence of the disease, the mode of the infection of the different hosts, the life history of the incriminated parasites and their pathological effects on the human subject, have been considered.

3. The symptomatology, treatment, diagnosis and prognosis of the disease have also been discussed generally and as fully as possible.

4. Consideration has also been given the different known varieties of snail "carriers", and points in connection with their distribution in the world, and the Sudan, their habitat, and the specific nature of the infection they carry, have been noted.

5. Special reference has been made to the incidence of Schistosomiasis in the Sudan.

6. For the purpose of illustration, a number of cases occurring among school-boys have been

selected, in order to show the type of disease found in a non-irrigated area of that country, and the symptomatology, diagnosis, and treatment of these cases have been given in detail.

7. Particular attention has been paid to the great value of Antimony Tartrate treatment, and the beneficial effects which have accrued in the treatment, prophylaxis, and eradication of the disease, since its introduction. Other forms of treatment and drugs have also been compared and described.

8. Prophylactic methods, such as may be, and are, applied in the Sudan and in the world in general, have been discussed at length, and the various difficulties encountered, racial, economic, and religious, in regard to their application, mentioned.

9. In conclusion it has been pointed out that although many problems remain yet to be solved, the future in regard to this serious disease, and its effects on the human race, is not unhopeful.

Acknowledgements.

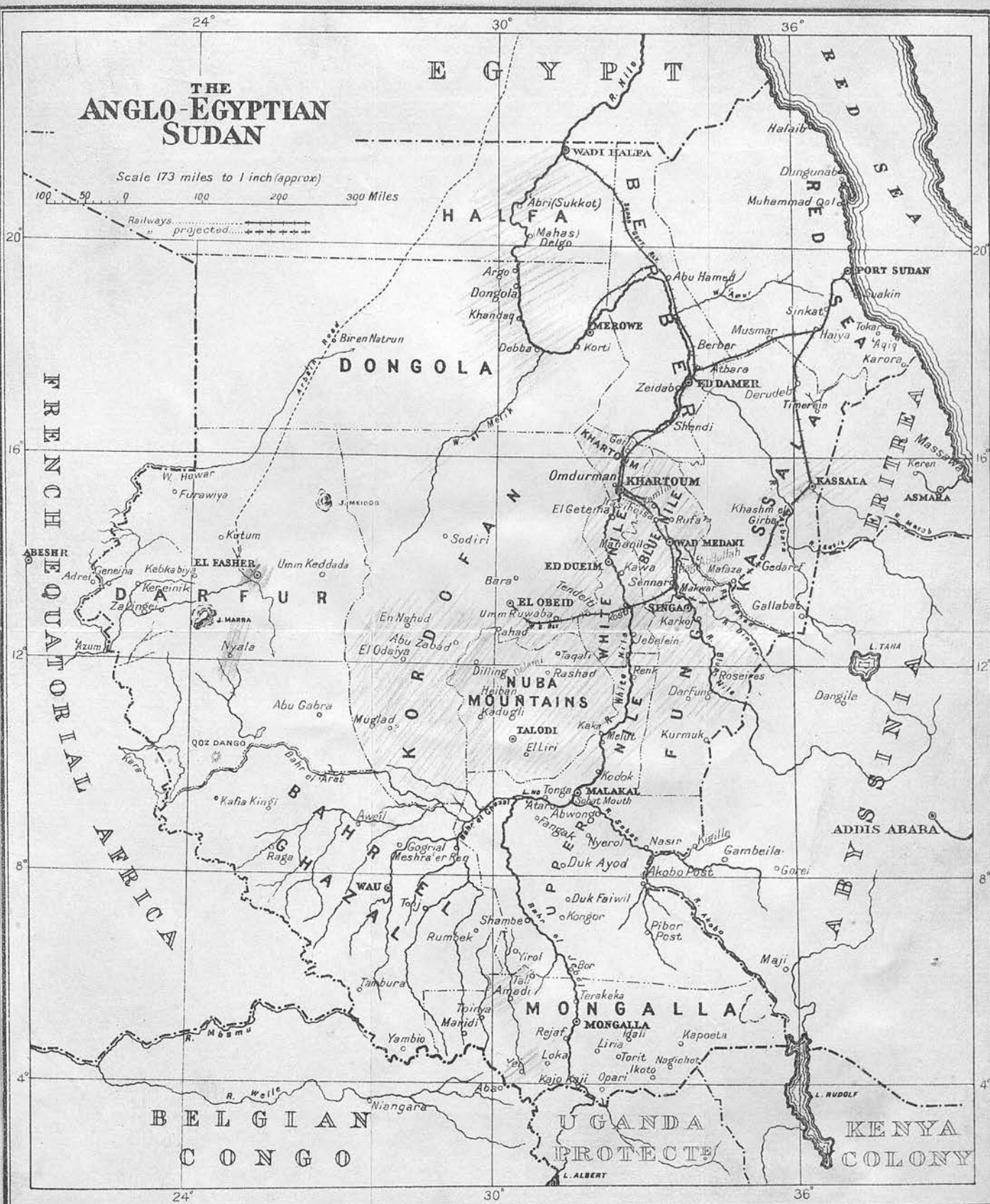
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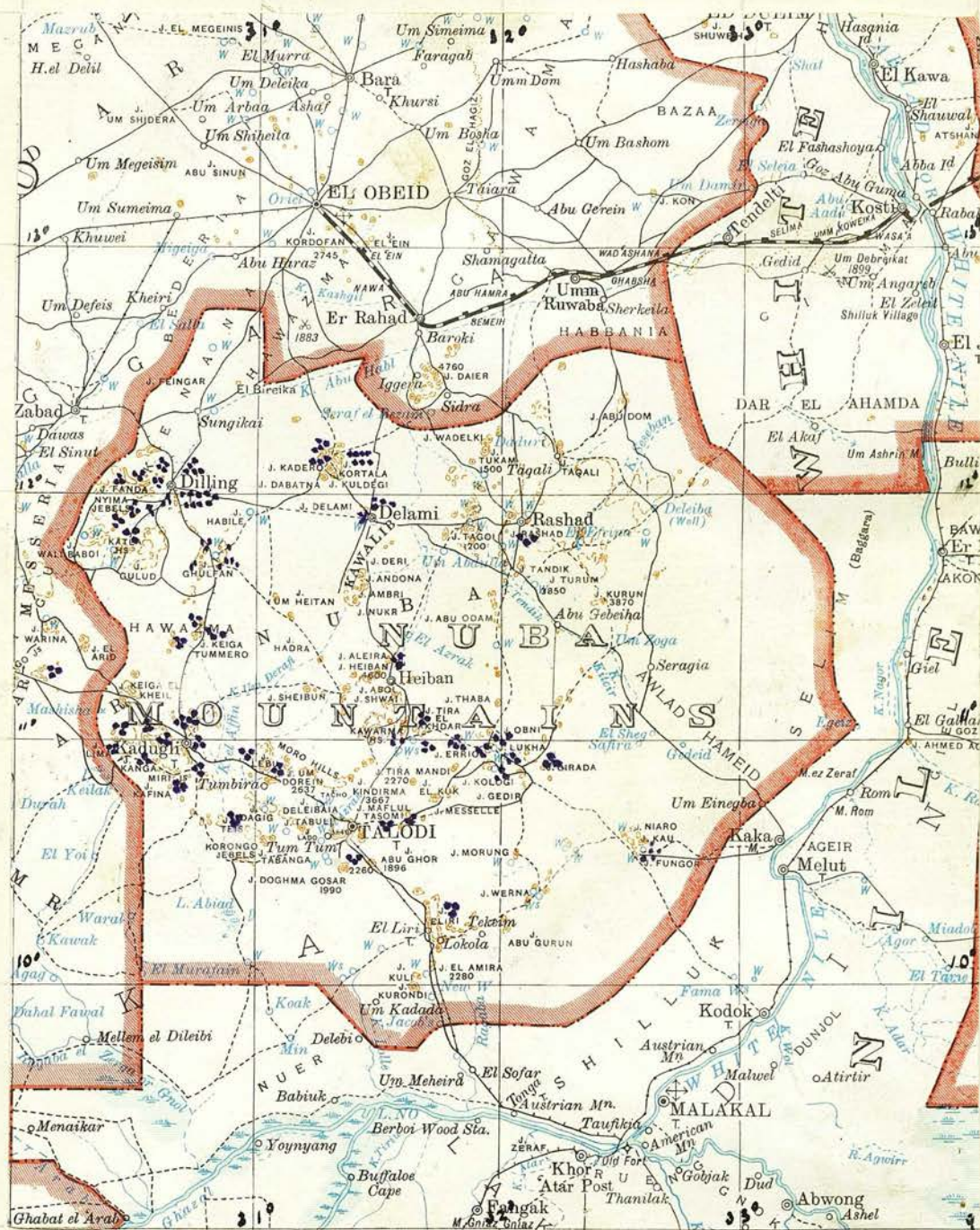
Printed at the Geographical Section, General Staff, War Office, 1921
Rev. 2nd Sep. 1926 & Sep. 1927. & Sep. 1928.

SURVEY DEPT KRANTDUM. NOV 1920.

graphical Section General Staff War Office, 1921
3 Sept 1927 & Sept 1928.

To show approximate distribution of Schistosome
in the Sudan.
affected areas coloured in red.

Survey Dept. Khartoum, Kh.



Scale $\frac{1}{3,000,000}$ To show distribution of *Bulbargia* in Kuba Mountain
1 inch = 49.35 miles 31° province 32° 33° By permission P. 190.

330 By permission P. 190. SDE

Notes.

* Leiper's latest dictum 1918 R.A.M.C. Journal XXX. No. 3. 235-60. Bilharz discovered the worm in 1851 which he named Distoma Haematobium, but which was renamed Bilharzia in honour of its discoverer by Cobbold. In 1858 Welland had created the genus Schistosoma for the worm Distoma Haematobium of Bilharz and Von Seibold. Leiper says that the generic name Bilharzia which conformed to the generally accepted views on nomenclature in those days, should stand as a perpetuation of the name of the discoverer.

Manson, Tropical Diseases, 7th Edition states that although Cobbold proposed the name Bilharzia in honour of the discoverer in 1859, Weinland had previously given the name Schistosoma to the genus and this is generally accepted by zoologists as the proper generic term.

+ Although these enlarged spleens, generally of malarial origin, are so extremely common, they appeared to have little effect on the after life of the children. It has been observed that as they grow older, except for a minority of cases, the spleens gradually grow normal in size.

Another interesting point is the apparent immunity these people have to malaria. If, say,

50 people from the Northern Sudan, taken from districts where malaria is known to occur, and 50 Nubawis, are put together to work in a malarious Southern district, as the Nuba Mountains Province, 50% of the Northern people will become ill with malaria and be incapacitated for work, whereas only about 5% of the Nubawis will become effected in the same way.

This apparent immunity to Malaria has been noticed among other Southern Sudanese tribes also.

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